

## INVENTOR SEARCH

=> fil capl; d que 11; d que 145  
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FILE COVERS 1907 - 14 Dec 2006 VOL 145 ISS 25  
 FILE LAST UPDATED: 13 Dec 2006 (20061213/ED)

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 'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L1 1 SEA FILE=CAPLUS ABB=ON US2003-661458/APPS

L2 141 SEA FILE=CAPLUS ABB=ON PACE G7/AU  
 L3 11003 SEA FILE=CAPLUS ABB=ON SMITH M7/AU  
 L4 1 SEA FILE=REGISTRY ABB=ON MORPHINE/CN  
 L5 1 SEA FILE=REGISTRY ABB=ON FENTANYL/CN  
 L6 1 SEA FILE=REGISTRY ABB=ON SUFENTANYL/CN  
 L7 1 SEA FILE=REGISTRY ABB=ON ALFENTANYL/CN  
 L8 1 SEA FILE=REGISTRY ABB=ON OXYMORPHONE/CN  
 L9 1 SEA FILE=REGISTRY ABB=ON HYDROMORPHONE/CN  
 L10 1 SEA FILE=REGISTRY ABB=ON OXYCODONE/CN  
 L11 31087 SEA FILE=CAPLUS ABB=ON (L5 OR L6 OR L7 OR L8 OR L9 OR L10)  
 L12 1073 SEA FILE=CAPLUS ABB=ON L11  
 L13 12914 SEA FILE=CAPLUS ABB=ON OPIOIDS/CT  
 L14 12914 SEA FILE=CAPLUS ABB=ON L14(L) KAPPA/OBI  
 L15 1209 SEA FILE=CAPLUS ABB=ON L14(L) MU/OBI  
 L16 12944 SEA FILE=CAPLUS ABB=ON AGONISTS/OBI  
 L17 56591 SEA FILE=CAPLUS ABB=ON L15(L) L17  
 L18 368 SEA FILE=CAPLUS ABB=ON L16(L) L17  
 L19 454 SEA FILE=CAPLUS ABB=ON L16(L) L17  
 L37 39125 SEA FILE=CAPLUS ABB=ON DRUG INTERACTIONS-OLD, NT/CT  
 L38 4450 SEA FILE=CAPLUS ABB=ON DRUG DELIVERY SYSTEMS-OLD/CT (L) COMB7/OB  
 L39 16989 SEA FILE=CAPLUS ABB=ON COMBINATION CHEMOTHERAPY/CT  
 L40 5480 SEA FILE=CAPLUS ABB=ON COMB7/OBI (L) PHARMAC7/OBI  
 L42 552 SEA FILE=CAPLUS ABB=ON (L12 OR L19) (L) (COMB7/OBI OR COADMIN7/OB  
 BI OR CODRUG7/OBI OR CONCOMITANT7/OBI OR CONCURRENT7/OBI OR  
 BLEND7/OBI OR MIXTURE7/OBI)  
 L43 82 SEA FILE=CAPLUS ABB=ON (L13 OR L18) (L) (COMB7/OBI OR COADMIN7/OB  
 BI OR CODRUG7/OBI OR CONCOMITANT7/OBI OR CONCURRENT7/OBI OR

1

BLEND7/OBI OR MIXTURE7/OBI)  
 L45 5 SEA FILE=CAPLUS ABB=ON ((L42 AND L43) OR (L12 OR L19) AND  
 (L13 OR L18) AND (L37 OR L38 OR L39 OR L40)) AND (L2 OR L3)

=> e 11,145

L210 5 (L1 OR L45)

=> fil embase; d que 181

FILE 'EMBASE' ENTERED AT 11:10:14 ON 14 DEC 2006  
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FILE COVERS 1974 TO 13 Dec 2006 (20061213/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L46 83 SEA FILE=EMBASE ABB=ON PACE G7/AU  
 L47 8120 SEA FILE=EMBASE ABB=ON SMITH M7/AU  
 L48 53452 SEA FILE=EMBASE ABB=ON MORPHINE/CT  
 L49 26736 SEA FILE=EMBASE ABB=ON FENTANYL/CT OR FENTANYL CITRATE/CT  
 L50 4395 SEA FILE=EMBASE ABB=ON SUFENTANYL/CT OR SUFENTANYL CITRATES/CT  
 L51 4482 SEA FILE=EMBASE ABB=ON ALFENTANYL/CT  
 L52 805 SEA FILE=EMBASE ABB=ON OXYMORPHONE/CT  
 L53 2957 SEA FILE=EMBASE ABB=ON HYDROMORPHONE/CT  
 L54 3754 SEA FILE=EMBASE ABB=ON OXYCODONE/CT  
 L72 493 SEA FILE=EMBASE ABB=ON L54(L) (CB OR IT)/CT  
 L80 10397 SEA FILE=EMBASE ABB=ON (L48 OR L49 OR L50 OR L51 OR L52 OR  
 L53) (L) (CB OR IT)/CT  
 L81 5 SEA FILE=EMBASE ABB=ON (L46 AND L47) OR (L80 AND L72 AND (L46  
 OR L47))

=> fil drugu; d que 196

FILE 'DRUGU' ENTERED AT 11:10:15 ON 14 DEC 2006  
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FILE LAST UPDATED: 11 DEC 2006 <20061211/UP>  
 >>> DERMENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<  
 >>> THESAURUS AVAILABLE IN /CT <<<

L5 1 SEA FILE=REGISTRY ABB=ON MORPHINE/CN  
 L6 1 SEA FILE=REGISTRY ABB=ON FENTANYL/CN  
 L7 1 SEA FILE=REGISTRY ABB=ON SUFENTANYL/CN  
 L8 1 SEA FILE=REGISTRY ABB=ON ALFENTANYL/CN  
 L9 1 SEA FILE=REGISTRY ABB=ON OXYMORPHONE/CN  
 L10 1 SEA FILE=REGISTRY ABB=ON HYDROMORPHONE/CN  
 L11 1 SEA FILE=REGISTRY ABB=ON OXYCODONE/CN

2

L85 2 SEA FILE=DRUGU ABB=ON PACE G7/AU  
 L86 1100 SEA FILE=DRUGU ABB=ON SMITH M7/AU  
 L87 9457 SEA FILE=DRUGU ABB=ON (L5 OR L6 OR L7 OR L8 OR L9 OR L10)  
 L88 269 SEA FILE=DRUGU ABB=ON L11  
 L89 19705 SEA FILE=DRUGU ABB=ON MORPHINE/CT  
 L90 11240 SEA FILE=DRUGU ABB=ON FENTANYL/CT  
 L91 2280 SEA FILE=DRUGU ABB=ON SUFENTANYL/CT  
 L92 2680 SEA FILE=DRUGU ABB=ON ALFENTANYL/CT  
 L93 252 SEA FILE=DRUGU ABB=ON OXYMORPHONE/CT  
 L94 866 SEA FILE=DRUGU ABB=ON HYDROMORPHONE/CT  
 L95 986 SEA FILE=DRUGU ABB=ON OXYCODONE/CT  
 L96 9 SEA FILE=DRUGU ABB=ON (L85 AND L86) OR ((L85 OR L86) AND (L87  
 OR L89 OR L90 OR L91 OR L92 OR L93 OR L94) AND (L88 OR L95))

=> fil wpi; d que 1110; d que 1123

FILE 'WPI' ENTERED AT 11:10:16 ON 14 DEC 2006  
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FILE LAST UPDATED: 8 DEC 2006 <20061208/UP>  
 MOST RECENT THOMSON SCIENTIFIC UPDATE: 200679 <200679/DW>  
 DERMENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> YOU ARE IN THE NEW AND ENHANCED DERMENT WORLD PATENTS INDEX <<<

>>> FOR DETAILS ON THE NEW AND ENHANCED DERMENT WORLD PATENTS INDEX

PLEASE VISIT:  
[http://www.stn-international.de/stndatabases/details/dwpi\\_r.html](http://www.stn-international.de/stndatabases/details/dwpi_r.html) <<<

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 PLEASE VISIT:  
[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf)

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<http://scientific.thomson.com/support/patents/coverage/latestupdates/>

PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE  
[http://www.stn-international.de/stndatabases/details/ipc\\_reform.html](http://www.stn-international.de/stndatabases/details/ipc_reform.html) and  
<http://scientific.thomson.com/media/scpoff/ipcidwpi.pdf>

>>> FOR DETAILS ON THE NEW AND ENHANCED DERMENT WORLD PATENTS INDEX  
 PLEASE SEE

[http://www.stn-international.de/stndatabases/details/dwpi\\_r.html](http://www.stn-international.de/stndatabases/details/dwpi_r.html) <<<

>>> YOU ARE IN THE NEW AND ENHANCED DERMENT WORLD PATENTS INDEX <<<  
 'BI ABEX' IS DEFAULT SEARCH FIELD FOR 'WPI' FILE

L108 79 SEA FILE=WPI ABB=ON PACE G7/AU  
 L109 2413 SEA FILE=WPI ABB=ON SMITH M7/AU  
 L110 1 SEA FILE=WPI ABB=ON L108 AND L109

L108 79 SEA FILE=WPI ABB=ON PACE G7/AU  
 L109 2413 SEA FILE=WPI ABB=ON SMITH M7/AU

3

L111 3147 SEA FILE=WPI ABB=ON MORPHINE/BI, ABEX OR FENTANYL/BI, ABEX OR  
 ALFENTANYL/BI, ABEX OR SUFENTANYL/BI, ABEX OR OXYMORPHONE/BI, ABEX  
 OR MR22593/BI, ABEX OR MR2 2593/BI, ABEX OR HYDROMORPHONE/BI, ABEX  
 X  
 L112 4 SEA FILE=WPI ABB=ON OXYCODONE7/CN  
 L113 431 SEA FILE=WPI ABB=ON L112/DCR  
 L114 4 SEA FILE=WPI ABB=ON (RABAO0/SDCN OR RACDH7/SDCN OR RA0FCO/SDC  
 N OR R06854/SDCN OR R16303/SDCN OR 103043-1-0-0/DCSE OR  
 103043-1-1-0/DCSE OR 103043-1-2-0/DCSE OR 758270-1-0-0/DCSE)  
 L115 435 SEA FILE=WPI ABB=ON L114 OR L113  
 L116 513 SEA FILE=WPI ABB=ON OXYCODONE/BI, ABEX  
 L117 198 SEA FILE=WPI ABB=ON MU OPIOIDS/BI, ABEX  
 L118 166 SEA FILE=WPI ABB=ON KAPPA/BI, ABEX (1W) OPIOIDS/BI, ABEX  
 L119 12146 SEA FILE=WPI ABB=ON B14-L01/MC OR C14-L01/MC  
 L120 100 SEA FILE=WPI ABB=ON L117 (2A) AGONISTS/BI, ABEX OR (L117 AND  
 L119)  
 L121 102 SEA FILE=WPI ABB=ON L118 (2A) AGONISTS/BI, ABEX OR (L118 AND  
 L119)  
 L122 486502 SEA FILE=WPI ABB=ON (W782 OR P867)/MO, M1, M2, M3, M4, M5, M6 OR  
 A61K045/IPC OR (B12-C09 OR C12-C09 OR B14-S09 OR C14-S09)/MC  
 L123 4 SEA FILE=WPI ABB=ON (L108 OR L109) AND (L111 OR L120) AND  
 (L115 OR L116 OR L121) AND L122

=> e 1110,1123

L211 4 (L110 OR L123)

=> fil medl; d que 1163

FILE 'MEDLINE' ENTERED AT 11:10:19 ON 14 DEC 2006

FILE LAST UPDATED: 13 Dec 2006 (20061213/UP). FILE COVERS 1950 TO DATE.

In preparation for the annual MEDLINE reload, the National Library of Medicine (NLM) has suspended delivery of regular updates as of November 15, 2006. In-process and in-data-review records will resume delivery on November 21, 2006, and will continue to be added to MEDLINE until December 17, 2006.

On December 17, 2006, all regular MEDLINE updates from November 15 to December 16 will be added to MEDLINE, along with 2007 Medical Subject Headings (MeSH(R)) and 2007 tree numbers.

The annual reload will be available in early 2007.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L144( 94) SEA FILE=MEDLINE ABB=ON PACE G7/AU  
 L145( 10732) SEA FILE=MEDLINE ABB=ON SMITH M7/AU  
 L146( 0) SEA FILE=MEDLINE ABB=ON L144 AND L145  
 L147( 28104) SEA FILE=MEDLINE ABB=ON MORPHINE/CT  
 L148( 10382) SEA FILE=MEDLINE ABB=ON FENTANYL/CT  
 L149( 294) SEA FILE=MEDLINE ABB=ON OXYMORPHONE/CT  
 L150( 704) SEA FILE=MEDLINE ABB=ON HYDROMORPHONE/CT  
 L151( 540) SEA FILE=MEDLINE ABB=ON OXYCODONE/CT  
 L152( 124991) SEA FILE=MEDLINE ABB=ON LUNG DISEASES, OBSTRUCTIVE-NT/CT  
 L153( 5936) SEA FILE=MEDLINE ABB=ON BRONCHIECTASIS-NT/CT

4

L154( 570864)SEA FILE-MEDLINE ABB-ON TUBERCULOSIS, PULMONARY-NT/CT  
 L155( 3460)SEA FILE-MEDLINE ABB-ON BRONCHOPNEUMONIA/CT  
 L156( 3610)SEA FILE-MEDLINE ABB-ON LARYNGITIS-NT/CT  
 L157( 11628)SEA FILE-MEDLINE ABB-ON SINUSITIS-NT/CT  
 L158( 13173)SEA FILE-MEDLINE ABB-ON PULMONARY FIBROSIS/CT  
 L159( 1561)SEA FILE-MEDLINE ABB-ON SARCOIDOSIS, PULMONARY/CT  
 L160( 113614)SEA FILE-MEDLINE ABB-ON LUNG NEOPLASMS-NT/CT  
 L161( 12766)SEA FILE-MEDLINE ABB-ON SLEEP APNEA SYNDROMES-NT/CT  
 L162( 0)SEA FILE-MEDLINE ABB-ON( L144 OR L145) AND (L147 OR L148 OR  
 L149 OR L150 OR L151) AND (L152 OR L153 OR L154 OR L155 OR  
 L156 OR L157 OR L158 OR L159 OR L160 OR L161)  
 L163 0 SEA FILE-MEDLINE ABB-ON L146 OR L162

>> dup rem 196,1210,1211,181

FILE 'DRUGU' ENTERED AT 11:10:37 ON 14 DEC 2006  
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FILE 'EMBASE' ENTERED AT 11:10:37 ON 14 DEC 2006

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PROCESSING COMPLETED FOR L96

PROCESSING COMPLETED FOR L210

PROCESSING COMPLETED FOR L211

PROCESSING COMPLETED FOR L81

L212 16 DUP REM L96 L210 L211 L81 (7 DUPLICATES REMOVED)

ANSWERS '1-9' FROM FILE DRUGU

ANSWERS '10-13' FROM FILE CAPLUS

ANSWER '14' FROM FILE WPIX

ANSWERS '15-16' FROM FILE EMBASE

>> d ibid ed abs 1-16

L212 ANSWER 1 OF 16 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN DUPLICATE 2

ACCESSION NUMBER: 2005-27268 DRUGU P S Full-text

TITLE: Ventilatory responses of healthy subjects to intravenous

combinations of morphine and oxycodone under imposed

hypercapnic and hypoxemic conditions.

AUTHOR: Ladd L A; Kam P C; Williams D B; Wright A W B; Smith M

T; Mather L E

CORPORATE SOURCE: Univ. Sydney; Sigma-Pharmaceuticals; Univ. Queensland

LOCATION: Brisbane; Melbourne, Austr.

SOURCE: Br. J. Clin. Pharmacol. (59, No. 5, 524-35, 2005) 5 Fig. 2 Tab.

37 Ref.

CODEN: BCPHWM ISSN: 0306-5251

AVAIL. OF DOC.: Department of Anaesthesia and Pain Management, University of

Sydney at Royal North Shore Hospital, St Leonards, NSW 2065,

Australia. (L.E.M.). (e-mail: lmather@med.usyd.edu.au).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 2005-27268 DRUGU P S Full-text

AB I.v. infusions of morphine sulfate (MOR) or oxycodone HCl (OXH) or their combination decreased the hypercapnic response and VE55 (i.e., mean minute ventilation at PTCO2=55 mmHg) to a similar degree in a randomized, placebo-controlled, double-blind, crossover study of 12 male volunteers. There was no consistent treatment effect on the hypoxemic response. OXH was associated with drowsiness, tingling, warm feeling, itching, and nausea. These findings suggest that no unexpected or disproportionate effects are expected of MOR and OXH treatments that might impede their use in combination for pain management.

ABEX Methods 12 Male volunteers (aged 18-45 yr) randomly received 1-hr i.v. infusions of placebo, MOR (7.5, 10, and 15 mg, M10, M15, and M15, respectively), OXH (5, 7.5, 10, and 15 mg, O5-O15, respectively), or their combination in dose ratios of 1:1, 1:1, and 2:1, in a crossover manner. Results Subjective side-effects increased with increasing OXH doses. Drowsiness, tingling, and warm feeling were mostly mild and random, although some subjects tended to experience recurring side-effects (e.g., itching or nausea). A consistent treatment effect was not demonstrated for slope or intercept of the hypoxemic response. There was a consistent and similar decrease in slope of the hypercapnic response during all active drug treatments (DT), with general recovery after treatment. There was also a consistent decrease of VE55 during all treatments, with partial recovery after DT, but not between active DT. During DT, VE55 decreased to a mean of 74% of the respective values before DT (74%, 68%, 69%, 68%, and 61% for M15, M10/O5, M7.5/O7.5, M5/O10, and O15, respectively). After DT, mean values of VE55 were 75%, 73%, 78%, 76%, and 75% of the respective values before DT. Drug and metabolite AUC 0-120 hr were linearly proportional to dose and did not differ between drugs. Although there were differences in mean plasma drug concentrations between subjects, there were no differences between treatments during infusion; differences were found between treatments after infusion, with concentrations being directly correlated with the OXH dose. VE55 was the most sensitive ventilatory response variable for comparing the individuals and treatments in relation to drug plasma concentrations. (ABD/Y230)

L212 ANSWER 2 OF 16 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN DUPLICATES 4

ACCESSION NUMBER: 2000-12785 DRUGU P S Full-text

TITLE: Co-administration of sub-antinoceptive doses of oxycodone

and morphine produces marked antinoceptive synergy with

reduced CNS side effects in rats.

AUTHOR: Ross F B; Wallis S C; Smith M T

CORPORATE SOURCE: Univ. Queensland

LOCATION: Brisbane, Austr.

SOURCE: Pain (44, No. 2-3, 421-28, 2000) 4 Fig. 24 Ref.

CODEN: PAINDB ISSN: 0304-3959

AVAIL. OF DOC.: School of Pharmacy, The University of Queensland, St Lucia,

Brisbane, Queensland 4072, Australia. (M.T.S.). (e-mail:

Marc.smith@pharmacy.uq.edu.au).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 2000-12785 DRUGU P S Full-text

AB The effects of i.c.v., i.p. and s.c. oxycodone hydrochloride (Boots) and

morphine hydrochloride on nociception were studied in rats. Co-administration

of oxycodone and morphine increased the levels of antinociception.

Behaviorally, rats that received equipotent doses of either opioid alone were

markedly sedated. The results suggested that co-administration of sub-

analgesic doses of oxycodone and morphine could provide excellent pain relief

with a reduction in opioid related CNS side effects.

4

6

ABEX Marked antinociceptive synergy was seen in Sprague-Dawley and Dark Agouti rats following sub-antinoceptive doses of oxycodone or morphine, irrespective of whether they were given i.c.v., i.p. or s.c. Sub-antinoceptive doses of either oxycodone or morphine alone to rats produced levels of antinociception similar to pre-dosing baseline levels. In Sprague-Dawley rats i.c.v. oxycodone at 40 nmol and morphine at 15 nmol caused a rapid onset (by 10 min) of maximum possible antinociception (MPE) which decreased relatively slowly (mean level of antinociception, greater than 50% of MPE at 3 hr). Pretreatment with naloxomazine or nor-BNI 24 hr prior to i.c.v. oxycodone 40 nmol plus morphine 15 nmol resulted in a decrease in the levels of antinociception. In Dark Agouti rats i.p. oxycodone at 571 nmol plus morphine at 621 nmol resulted in 100% MPE by 10 min. The mean levels of antinociception remained high for the 1st 2 hr of the experimental period and then decreased to 65% MPE by 3 hr postdosing. Oxycodone 571 nmol i.p. with 310 nmol morphine or oxycodone 285 nmol plus 621 nmol morphine resulted in maximum antinociception by 15 min but the duration of action was reduced to 2 hr. Co-administration of oxycodone or morphine in sub-antinoceptive doses neither strain of rat showed any adverse behavioral effects such as sedation, incontinence or catatonias. In Dark Agouti rats the ED50 doses of s.c. oxycodone and morphine were 2.8 and 8.5 mg/kg, respectively. Behaviorally rats given single s.c. morphine or oxycodone in doses larger than the ED50 were sedated. Co-administration of sub-antinoceptive doses of oxycodone and morphine produced synergistic levels of pain relief. (LL)

L212 ANSWER 3 OF 16 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN DUPLICATE 6

ACCESSION NUMBER: 1994-22863 DRUGU P S Full-text

TITLE: The antinociceptive potencies of oxycodone, noroxycodone and

morphine after intracerebroventricular administration to

rats.

AUTHOR: Leow K P; Smith M T

CORPORATE SOURCE: Univ. Queensland

LOCATION: Brisbane, Australia

SOURCE: Life Sci. (54, No. 17, 1229-36, 1994) 2 Fig. 1 Tab. 20 Ref.

CODEN: LIFSAK ISSN: 0024-3205

AVAIL. OF DOC.: Department of Pharmacy, The University of Queensland, St

Lucia, Queensland 4072, Australia. (M.T.S.).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 1994-22863 DRUGU P S Full-text

AB In rats, i.c.v. administration of noroxycodone (NOR, Du-Pont-Merck) or

oxycodone HCl (OXY, Sigma-Chemical) had a more potent antinociceptive effect

than that of i.c.v. morphine HCl (MOR). Administration of i.c.v. naloxone

HCl (Sigma-Chemical) abolished the antinociceptive response produced by the

subsequent administration of OXY, MOR or NOR, indicating that the

antinociceptive effects of these 3 drugs are mediated by opioid receptors.

NOR also produced excitatory effects throughout the antinociceptive range.

The severity of which was reduced, but not abolished, by prior administration

of i.c.v. naloxone. As excitatory effects have not been observed in patients

receiving OXY, it is unlikely that NOR contributes to the analgesic activity

of OXY administered systemically.

ABEX In male Sprague-Dawley rats (250 g), the ED50 value for i.c.v. MOR was

34 nmol. Corresponding ED50 values for i.c.v. OXY and MOR were 78 and

200 nmol, respectively. Antinociceptive potencies of OXY and MOR

relative to MOR, estimated using the ED50 values, were 0.44 and 0.17,

respectively. After i.c.v. MOR, the antinociceptive response comprised 2

distinct phases. During phase 1, antinociception commenced at 15-30 min,

peaked at 45-60 min and decreased at 75 min. Phase 2 antinociception peaked at 90 min and decreased throughout the remainder of the 3-hr observation period. During phase 2 antinociception, rats were incontinent. Only phase 1 antinociception was observed in rats given OXY. Onset of antinociception was very rapid with peak values occurring at 7-15 min post-dosing. When MOR was administered, 2 antinociceptive phases were observed in a manner analogous to that observed after i.c.v. MOR. Time to achieve maximum antinociception was significantly shorter for OXY (9.3 min) than for MOR (31.8 min) or NOR (34.6 min). At equipotent doses, the mean duration of antinociception was significantly shorter for i.c.v. OXY (114 min) than for i.c.v. MOR and NOR (180 min). Naloxone (55 nmol) given 15 min prior to i.c.v. opioid agonist significantly reduced the antinociceptive response of the respective opioid agonist administered alone. NOR also produced allodynia, excessive facial grooming, tremor, Straub tail and myoclonic jerks. The severity of these effects was reduced but not eliminated by subsequent naloxone. Grand mal seizures then death occurred in 2 rats given 432 nmol of MOR. (SAB)

L212 ANSWER 4 OF 16 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN

ACCESSION NUMBER: 2000-44276 DRUGU P S Full-text

TITLE: Incomplete, asymmetric, and route-dependent cross-tolerance

between oxycodone and morphine in the Dark Agouti rat.

AUTHOR: Nielsen C K; Ross F B; Smith M T

CORPORATE SOURCE: Univ. Queensland

LOCATION: Brisbane, Austr.

SOURCE: J. Pharmacol. Exp. Ther. (295, No. 1, 91-99, 2000) 4 Fig. 4 Tab.

29 Ref.

CODEN: JPETAB ISSN: 0022-3565

AVAIL. OF DOC.: School of Pharmacy, The University of Queensland, St. Lucia,

Queensland 4072, Australia. (M.T.S.). (e-mail:

m.smith@pharmacy.uq.edu.au).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 2000-44276 DRUGU P S Full-text

AB The antinociceptive effects of bolus i.v. or i.c.v. oxycodone HCl (OX,

Tasmanian Alkaloids) or morphine sulfate (MP) were determined OX- and MP-

tolerant rats. In MP-tolerant rats, i.c.v. OX did not induce cross-tolerance

whereas i.v. OX induced a low degree of cross-tolerance. In OX-tolerant rats,

both i.c.v. and i.v. induced a high degree of cross-tolerance. It was

concluded that after parenteral but not supraspinal administration, OX is

metabolized to a mu-opioid agonist metabolite, thereby explaining asymmetric

and incomplete cross-tolerance between OX and MP.

ABEX Methods Dark Agouti rats (200 g) received i.v. infusion of OX (2.5 or

5 mg/day) or MP (10 or 20 mg/day) until rats were completely tolerant

followed by 12-hr washout period. OX-tolerant, MP-tolerant and

drug-naïve rats received either bolus i.v. OX (79-1585 nmol) or MP

(350-3504 nmol) or bolus i.c.v. OX (22-132 nmol) or MP (18-150 nmol).

Results Complete antinociceptive tolerance was produced by 48 hr in

naïve rats following chronic i.v. infusion of OX (2.5 mg/day) and MP (10

mg/day). Chronic i.v. infusion of OX (5 mg/day) induced tolerance in

naïve, MP-tolerant and OX-tolerant rats after 72 hr, 48 hr and 8 hr,

respectively. Chronic i.v. infusion of MP (20 mg/day) induced tolerance

in naïve, OX-tolerant and MP-tolerant rats after 84 hr, 36 hr and 12 hr,

respectively. Equipotent antinociception was produced by chronic i.v. OX

and MP in doses of 2.5 mg/day and 10 mg/day, respectively, and tolerance

was established over a similar time frame. In MP-tolerant rats, i.c.v.

OX did not affect the dose-response curve or ED50 of i.c.v. OX, whereas

AUTHOR: Wright A M E; Leow K P; Cramond T; Smith M T  
CORPORATE SOURCE: Univ. Queensland  
LOCATION: Brisbane, Australia  
SOURCE: Aust. J. Hosp. Pharm. (24, No. 2, 206, 1994)  
CODEN: AUHPAI ISSN: 0310-6810  
AVAIL. OF DOC.: Dept. of Pharmacy, The University of Queensland, Brisbane,  
Queensland, 4072, Australia.  
LANGUAGE: English  
DOCUMENT TYPE: Journal  
FIELD AVAIL.: AB; LA; CT  
FILE SEGMENT: Literature  
AN 1994-27116 DRUGU P Full-text  
The extent of serum protein binding of

AB The study aim was to determine the extent of serum protein binding of oxycodone (OX) and morphine (MO) in HSA and human albumin (HSA) glycoprotein (AAG). OX and MO bound primarily to HSA, although both drugs bound to AAG with a higher affinity than to albumin. A decrease in temperature or an increase in pH significantly increased the protein binding of both OX and MO. The serum protein binding of both opioids was independent of drug concentration in the therapeutic range (5-100 ng/ml), but was dependent on the protein concentration. It is unlikely that changes in serum protein concentrations associated with disease states such as renal or hepatic failure would alter the pharmacological effects of OX or MO due to the normally low extent of binding of both drugs. (congress abstract).

ABXX Methods Serum protein binding was determined *in vitro* by ultrafiltration. Binding studies were also performed using both purified HSA and AAG. Results OX and MO bound primarily to albumin although both drugs bound to AAG with a higher affinity than to albumin. At physiological pH and temperature, the mean serum protein binding of OX and MO were 45.1% and 35.3%, respectively. A decrease in temperature (from 37 deg to 23 deg) or an increase in pH (from 7.4 to 7.75-7.85) significantly increased the protein binding of both OX and MO, underlining the necessity to conduct protein binding studies at physiological pH and temperature. The serum protein binding of both opioids was independent of drug concentration in the therapeutic range (5-100 ng/ml) but was dependent on the protein concentration. In serum containing albumin and AAG concentrations within the normal ranges, the binding of both drugs to albumin and AAG would be in the ranges 31-39% and 5-10%, respectively, and the binding of morphine would be 26-34% and 4-5%, respectively. (SAB)

L212 ANSWER 7 OF 16 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN  
ACCESSION NUMBER: 1993-52909 DRUGU P Pull-text  
TITLE: Determination of the Serum Protein Binding of Oxycodone and  
Morphine Using Ultracfiltration  
AUTHOR: Leow K P; Wright A W B; Cramond T; Smith M T  
LOCATION: Brisbane, Australia  
SOURCE: Ther. Drug Monit. (15, No. 5, 440-47, 1993) 6 Tab. 23 Ref.  
CODEN: TDMODV ISSN: 0163-4356  
AVAIL. OF DOC.: Department of Pharmacy, University of Queensland, Brisbane,  
Queensland 4072, Australia.  
LANGUAGE: English  
DOCUMENT TYPE: Journal  
FIELD AVAIL.: AB; LA; CT; MPC  
KEYWORDS: MORPHINE  
KEYWORDS: OXYCODONE

AN 1993-52909 DRUGU B Pull-text  
AB Serum protein binding of both oxycodone (OX) and morphine (MO) was fairly low and independent of drug concentration in the therapeutic range, but increased with increasing levels of total protein and of purified HSA or human alpha<sub>2</sub>-acid glycoprotein (AAG, both Sigma-Chemical), in blood samples from healthy subjects. Albumin was the major binding protein for both OX and MO. Bound

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of OC and at least 65 µg of NOC. A significantly shorter duration of antinociception occurred after OC than after M or NOC. I.c.v. administration of NAL markedly reduced the degree of antinociception produced by the subsequent i.c.v. administration of OC and NOC, indicating that the antinociceptive effects of OC and NOC are mediated by opioid receptors. The effects of dose-dependent excitatory effects (allodynia, excessive facial grooming, tremor, Straub tail, myoclonic jerks, generalized seizures) were also observed in rats which receive i.c.v. NOC, the severity of which was reduced when NAL was administered by the i.c.v. route. The ED<sub>50</sub> of NAL (20 µg i.c.v.) = (RS4/RSV).

L212 ANSWER 9 OF 65 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STM  
ACCESSION NUMBER: 1994-06518 DRUGU P T Full-text  
TITLE: A New Metabolite of Oxycodone in Humans.  
AUTHOR: Ross F B; Cramond T; Smith M T  
CORPORATE SOURCE: Univ.Queensland  
LOCATION: Brisbane, Australia  
SOURCE: Clin Exp Pharmacol Physiol. [Suppl. 1, 63, 1993] 1.Ref.  
CODEN: CEXPE9 ISSN: 0305-1870  
AVAIL. OF DOC.: Department of Pharmacy, University of Queensland, Qld 4072,  
Australia.  
LANGUAGE: English  
DOCUMENT TYPE: Journal  
FIELD AVAIL.: AB; LA; CT: MPC  
ALFABET: ALFABET

AN 1994-06518 DRUGU P T Full-text  
AB The metabolism of oxycodone (OC), a semi-synthetic opioid derivative with a reported efficacy approximately 0.7 that of morphine for the management of cancer pain, was studied in 8 cancer patients receiving OC chronically and in 5 healthy volunteers after a single p.o. dose. Urinary recovery of OC, noroxycodone (NOC) and oxymorphone (OM) was only 25%. However, an unstable metabolite was found, that accounted for at least 50% of the OC dose, and was shown to be a catechol derivative of OM. (congress abstract).

ABEX As OC has low affinity for mu-opioid receptor ( $K_d$  more than 1 uM), it is postulated that OC's analgesic efficacy may be due to formation of 1 or more active metabolites. The current studies both in cancer patients receiving OC chronically (40 mg daily) and in healthy volunteers after a single oral dose (10 mg) showed that the mean total urinary recovery of OC, MOC and OM (conjugated and unconjugated) was 25%. Also, the OM urinary concentration was less than 0.5 ug/ml in all urine samples. After incubation of OC urine with beta-glucuronidase, a new metabolite accounting for at least 50% of the OC dose, appeared in the HPLC chromatogram. In healthy volunteers this new metabolite only appeared in the 2nd 12 hr period after dosing. This putative OC metabolite was difficult to isolate because it is unstable in acidic urine and in HPLC mobile phase. On the other hand, the chemical structure of this metabolite was consistent with the UV spectrum and with its mobility in organic fluids; it is a catechol derivative of OM. (854/RSV)

1212 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2006 ACS ON STM DUPLICATE 1  
ACCESSION NUMBER: 2005:219720 CAPLUS Pull-text  
DOCUMENT NUMBER: 142.274052  
TITLE: Methods and compositions using sub-analgesic doses of  
a  $\mu$  opioid agonist and oxycodeone for reducing the  
risk associated with the administration of opioid  
analgesics in patients with diagnosed or undiagnosed  
respiratory illness  
INVENTOR(S): Peca, Gary W.; Smith, Marce T.  
ASSIGNOR(S): VEA

SOURCE: U.S. Pat. Appl. Publ., 11 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE        |
|---|------|----------|-----------------|-------------|
| US 200503659  | A1   | 20050310 | US 2003-661458  | 20030910    |
| WO 200502621  | A1   | 20050314 | WO 2004-US29731 | 20040910    |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GR, OH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RU, SC, SD, SE, SG, SK, SL, SM, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |             |
| RW: BW, GH, GM, KE, LS, LM, MG, NA, SD, SE, SI, SK, TH, TZ, UG, ZM, ZW  |      |          |                 |             |
| AZ, BY, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, FR, GB, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RU, SC, SD, SE, SG, SK, SL, SM, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW  |      |          |                 |             |
| EP 1667723  | A1   | 20060614 | EP 2004-783810  | 20040910    |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK   |      |          |                 |             |
| PRIORITY APPL. INFO.:   |      |          | US 2003-661458  | A1 20030910 |
|   |      |          | WO 2004-US29731 | W 20040910  |

ED Entered STN: 11 Mar 2005

AB The invention discloses methods for reducing the risk associated with the administration of opioid analgesics in patients diagnosed or undiagnosed with respiratory illness by administering an analgesic composition comprising a sub-analgesic dosage of a  $\mu$ -opioid agonist selected from morphine, fentanyl, sufentanil, alfentanil, oxycodone and hydromorphone, or a pharmaceutically acceptable salt thereof, and a sub-analgesic dosage of oxycodone, which is a  $\kappa$ -opioid agonist, or a pharmaceutically acceptable salt thereof.

L212 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2006 ACS ON STN DUPLICATE 3

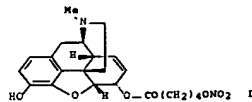
ACCESSION NUMBER: 2003:75712 CAPLUS Full-text  
 DOCUMENT NUMBER: 139:271069  
 TITLE: Methods and compositions including nitric oxide donors and opioid analgesics for pain relief  
 INVENTOR(S): Smith, Maree Therese; Brown, Lindsay; Harvey, Mark Bradford; Pullar, Williams, Craig McKenzie  
 PATENT ASSIGNER(S): The University of Queensland, Australia  
 SOURCE: PCT Int. Appl., 69 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 2003078437   | A1   | 20030925 | WO 2003-AU335   | 20030320 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GR, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PH, PL, PT, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |          |

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TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, LM, MG, NA, SD, SE, SI, SK, TH, TZ, UG, ZM, ZW, AM, AZ, BY, KO, KZ, MD, RU, TJ, TM, AT, BE, BG, BO, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TH, BF, BJ, CP, CO, CI, CM, GA, GH, GM, GU, GW, ML, MR, NE, SN, TD, TG  
 CA 2479098 A1 20030925 CA 2003-2479098 20030320  
 AU 2003209850 A1 20030929 AU 2003-209850 20030320  
 US 200319494 A1 20031127 US 2003-393050 20030320  
 EP 1495026 A1 20050112 EP 2003-744274 20030320  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK  
 JP 2005524676 T2 20050818 JP 2003-576442 20030320  
 CN 1703416 A 20051130 CN 2003-099228 20030320  
 PRIORITY APPL. INFO.:

OTHER SOURCE(S): MARPAT 139:271069  
 ED Entered STN: 26 Sep 2003  
 GI



AB Comps. and methods that induce, promote or otherwise facilitate pain relief are disclosed. These composites and methods comprise a nitric oxide donor which either directly or indirectly prevents, attenuates or reverses the development of reduced opioid sensitivity, together with a compound which activates the opioid receptor that is the subject of the reduced opioid sensitivity. The composites and methods prevent or alleviate pain, especially in neuropathic conditions and even more especially in peripheral neuropathic conditions such as painful diabetic neuropathy. The preferred nitric oxide donor is L-arginine, while the preferred compounds which activate the opioid receptor are morphine and oxycodone. Conjugate compounds comprising the nitric oxide donor and an opioid analgesic are also disclosed. Preparation of morphine-NO donor conjugates, e.g. 1, is also described.  
 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L212 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2006 ACS ON STN DUPLICATE 5  
 ACCESSION NUMBER: 1997:361742 CAPLUS Full-text  
 DOCUMENT NUMBER: 126:325531  
 TITLE: Production of analgesic synergy by co-administration of sub-analgesic doses of a  $\mu$ -opioid agonist and a  $\kappa$ -opioid agonist  
 INVENTOR(S): Smith, Maree; Ross, Fraser  
 PATENT ASSIGNER(S): University of Queensland, Australia; Lynx Project Limited; Smith, Maree; Ross, Fraser  
 SOURCE: PCT Int. Appl., 83 pp.  
 CODEN: PIXXD2

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DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO.          | DATE     |
|---|------|----------|--------------------------|----------|
| WO 9714438  | A1   | 19970424 | WO 1996-AU656            | 19961021 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GR, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                          |          |
| RW: KE, LS, LM, MG, NA, SD, SE, SI, SK, TH, TZ, UG, ZM, ZW  |      |          |                          |          |
| IE, IT, LU, MC, NL, PT, SE, SP, BJ, CP, CO  |      |          |                          |          |
| ZA 9608808 A 19970527 ZA 1996-8808 19961019   |      |          |                          |          |
| CA 2235375 AA 19970424 CA 1996-2235375 19961021   |      |          |                          |          |
| AU 9672076 A 19970507 AU 1996-72076 19961021  |      |          |                          |          |
| AU 706691 B2 19960624 19961021  |      |          |                          |          |
| EP 871488 A1 19981021 EP 1996-933277 19961021   |      |          |                          |          |
| EP 871488 B1 20050413 19961021  |      |          |                          |          |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI   |      |          |                          |          |
| CN 1204264 A 19990106 CN 1996-199071 19961021   |      |          |                          |          |
| CN 1104910 B 20030409 19961021  |      |          |                          |          |
| AT 292982 E 20050415 AT 1996-933277 19961021  |      |          |                          |          |
| ES 2241003 T3 20051016 ES 1996-933277 19961021  |      |          |                          |          |
| US 6310072 B1 20011030 US 1997-921187 19970829  |      |          |                          |          |
| PRIORITY APPL. INFO.:   |      |          | AU 1995-6038 A 19951019  |          |
|   |      |          | WO 1996-AU656 W 19961021 |          |

ED Entered STN: 11 Jun 1997

AB An analgesic composition comprises a sub-analgesic dosage of a  $\mu$ -opioid agonist or analog or derivative or pharmaceutically acceptable salts thereof and a sub-analgesic dosage of a  $\kappa$ -opioid agonist or analog or derivative or pharmaceutically acceptable salts thereof. The  $\mu$ -opioid agonist may be morphine, fentanyl, sufentanil, alfentanil, or hydromorphone; the  $\kappa$ -opioid agonist may be oxycodone.

L212 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2006 ACS ON STN

ACCESSION NUMBER: 2003:757520 CAPLUS Full-text  
 DOCUMENT NUMBER: 139:255390  
 TITLE: Method of treatment and prophylaxis of neuropathic condition  
 INVENTOR(S): Smith, Maree Therese; Brown, Lindsay  
 PATENT ASSIGNER(S): The University of Queensland, Australia  
 SOURCE: PCT Int. Appl., 87 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 2003077912   | A1   | 20030925 | WO 2003-AU336   | 20030320 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GR, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |          |

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PH, PL, PT, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, LM, MG, NA, SD, SE, SI, SK, TH, TZ, UG, ZM, ZW, AM, AZ, BY, KO, KZ, MD, RU, TJ, TM, AT, BE, BG, BO, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TH, BF, BJ, CP, CO, CI, CM, GA, GH, GM, GU, GW, ML, MR, NE, SN, TD, TG  
 AU 2003209851 A1 20030929 AU 2003-209851 20030320  
 US 2003199424 A1 20031023 US 2003-393056 20030320  
 PRIORITY APPL. INFO.:

ED Entered STN: 26 Sep 2003

AB The invention is involves the use of angiotensin II receptor 1 (AT1 receptor) antagonists for the treatment, prophylaxis, reversal and/or symptomatic relief of a neuropathic condition, especially a peripheral neuropathic condition such as painful diabetic neuropathy, in vertebrate animals and particularly in human subjects. The invention also discloses the use of AT1 receptor antagonists for preventing, attenuating or reversing the development of reduced opioid sensitivity, and more particularly reduced opioid analgesic sensitivity, in individuals and especially in individuals having, or at risk of developing, a neuropathic condition.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L212 ANSWER 14 OF 16 WPX COPYRIGHT 2006 THE THOMSON CORP ON STN  
 ACCESSION NUMBER: 2006-464147 [47] WPX  
 DOC. NO. CFI: C2006-145568 [47]

TITLE: Method of producing analgesia, useful to relieve pain e.g. moderate to severe cancer pain and post surgical pain, comprises administering a nitric oxide donor and an opioid analgesic

DERIVAT CLASS: B02  
 INVENTOR: SMITH M T  
 PATENT ASSIGNER: (UYU-C) UNIV QUEENSLAND  
 COUNTRY COUNT: 111

PATENT INFO ABBR.:

| PATENT NO    | KIND | DATE     | WEEK     | LA | PO | MAIN IPC |
|--------------|------|----------|----------|----|----|----------|
| WO 200606362 | A1   | 20060629 | (200647) | EN |    | B7[11]   |

APPLICATION DETAILS:

| PATENT NO    | KIND | APPLICATION    | DATE     |
|--------------|------|----------------|----------|
| WO 200606362 | A1   | WO 2005-AU1976 | 20051223 |

PRIORITY APPL. INFO: AU 2004-907352 20041224  
 ED 20060724  
 AN 2006-464147 [47] WPX  
 AB WO 200606362 A1 UPAB: 20060724

NOVELTY - Method of producing analgesia (A) in a subject comprises administering a nitric oxide donor (II) and an opioid analgesic, where (II) delivers nitric oxide (II) at a rate of 0.0002-2 nmol/kg/hour.  
 DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for new compounds of formula (I).  
 ACTIVITY - Analgesic.  
 MECHANISM OF ACTION - None given.  
 USE - (A) is useful to relieve pain (moderate to severe cancer pain, moderate to severe post surgical pain, pain following physical trauma, pain associated

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with cardiac infarction and inflammatory pain) (claimed). No biological data given.  
 ADVANTAGE - (A) enhances the endogenous production of nitroethiols and reduces the endogenous production of peroxynitrite.

L212 ANSWER 15 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005175148 EMBASE Full-text  
 TITLE: Co-administration of oxycodone and morphine and analgesic synergy re-examined [1] (multiple letters).  
 AUTHOR: Smith M.T.; De La Iglesia F.A.; Grath M.; Massalha W.; Pud D.; Adler R.; Eisenberg R.  
 CORPORATE SOURCE: F.A. De La Iglesia, University of Michigan, Medical School, Ann Arbor, MI, Australia. delaigf@umich.edu  
 SOURCE: British Journal of Clinical Pharmacology, (2005) Vol. 59, No. 4, pp. 486-488.  
 ISBN: 0304-5351 CODEN: BCPHEM  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal: Letter  
 FILE SEGMENT: 008 Neurology and Neurosurgery  
 037 Drug Literature Index  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 12 May 2005  
 Last Updated on STN: 12 May 2005  
 ED Entered STN: 12 May 2005  
 Last Updated on STN: 12 May 2005  
 DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L212 ANSWER 16 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 97021905 EMBASE Full-text  
 DOCUMENT NUMBER: 1997021905  
 TITLE: HIV-1 protease inhibitors: A review for clinicians.  
 AUTHOR: Deeks S.G.; Smith M.; Holodny M.; Kahn J.O.  
 CORPORATE SOURCE: Dr. J.O. Kahn, University of California, San Francisco General Hospital, 995 Potrero Ave, San Francisco, CA 94110, United States. jkahn@sfids.ucsf.edu  
 SOURCE: Journal of the American Medical Association, (1997) Vol. 277, No. 2, pp. 145-153.  
 Refs: 59  
 ISSN: 0098-7484 CODEN: JAMAAP  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal: General Review  
 FILE SEGMENT: 006 Internal Medicine  
 030 Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 15 Feb 1997  
 Last Updated on STN: 15 Feb 1997  
 ED Entered STN: 15 Feb 1997  
 Last Updated on STN: 15 Feb 1997

AB Objective: The clinical care of people infected with human immunodeficiency virus (HIV) has been substantially affected by the introduction of HIV-specific protease inhibitors (PIs). The 4 PIs available are zidovudine, zalcitabine, didanosine, and zalcitabine. Comparison studies have not been reported; therefore, an assessment of the available data to aid clinicians and patients in choosing appropriate treatment will be

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presented. Data Sources: A systematic review of peer-reviewed publications, abstracts from national and international conferences, and product registration information through September 1996. Study Selection and Data Extraction: Criteria used to select studies include their relevance to PIs, having been published in the English language, and pertinence for clinicians. Data quality and validity included the venue of the publication and relevance to clinical care. Data Synthesis: Oral administration of zidovudine, didanosine, or zalcitabine generates sustainable drug serum levels to effectively inhibit the protease enzyme; however, saquinavir may not generate sustained levels necessary to inhibit the protease enzyme. Patients treated with zidovudine, didanosine, or zalcitabine experience similar reductions in viral load and increases in CD4+ lymphocytes; smaller effects occur among those treated with saquinavir. Two randomized placebo-controlled studies conducted among patients with severe immune system suppression and substantial zidovudine treatment experience demonstrated reduced HIV disease progression and reduced mortality with PI treatment. Genotypic resistance to PIs occurs; the clinical relevance of resistance is unclear. The costs of these agents including required monitoring impose new and substantial costs. Conclusions: The PIs have emerged as critical drugs for people with HIV infection. Optimal use involves combination with reverse transcriptase inhibitors. Resistance develops to each agent, and cross-resistance is likely. These agents must be used at full doses with attention to ensuring patient compliance. The expense of these agents may be offset by forestalling disease progression and death and returning people to productive life. Selecting the initial PI must be individualized, and factors to consider include proven activity, possible toxicities, dosing regimens, drug interactions, and costs.

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## TEXT SEARCH

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 L8 1 SEA FILE-REGISTRY ABB-ON ALFENTANYL/CN  
 L9 1 SEA FILE-REGISTRY ABB-ON OXYMORPHONE/CN  
 L10 1 SEA FILE-REGISTRY ABB-ON HYDROMORPHONE/CN  
 L11 1 SEA FILE-REGISTRY ABB-ON OXYCODONE/CN  
 L12 31087 SEA FILE-CAPLUS ABB-ON (L5 OR L6 OR L7 OR L8 OR L9 OR L10)  
 L13 1073 SEA FILE-CAPLUS ABB-ON L11  
 L14 12914 SEA FILE-CAPLUS ABB-ON OPIOIDS/CT  
 L15 1209 SEA FILE-CAPLUS ABB-ON L14(L) KAPPA/OBI  
 L16 1944 SEA FILE-CAPLUS ABB-ON L14(L) MU/OBI  
 L17 56591 SEA FILE-CAPLUS ABB-ON AGONISTS/OBI  
 L18 368 SEA FILE-CAPLUS ABB-ON L15(L) L17  
 L19 454 SEA FILE-CAPLUS ABB-ON L15(L) L17  
 L20 19117 SEA FILE-CAPLUS ABB-ON RESPIRATORY TRACT/OBI  
 L21 76 SEA FILE-CAPLUS ABB-ON L20(L) CARCINOMA/OBI  
 L22 25232 SEA FILE-CAPLUS ABB-ON ASTHMA/OBI  
 L23 424 SEA FILE-CAPLUS ABB-ON BRONCHITIS/OBI OR BRONCHI?/OBI (L) DI  
 LATATION/OBI OR KARTAGENER/OBI  
 L24 28786 SEA FILE-CAPLUS ABB-ON TUBERCULOSIS/OBI  
 L25 4089 SEA FILE-CAPLUS ABB-ON BRONCHITIS/OBI  
 L26 120 SEA FILE-CAPLUS ABB-ON RESPIRATORY SYSTEM, NEOPLASM/CT  
 L27 35560 SEA FILE-CAPLUS ABB-ON LUNG, NEOPLASM/CT  
 L28 4982 SEA FILE-CAPLUS ABB-ON CHRONIC OBSTRUCTIVE PULMONARY/OBI OR  
 COPD/OBI  
 L29 7726 SEA FILE-CAPLUS ABB-ON BRONCHOPNEUMONIA/OBI OR PNEUMONIA/OBI  
 L30 136 SEA FILE-CAPLUS ABB-ON LARYNGITIS/OBI  
 L31 1101 SEA FILE-CAPLUS ABB-ON SINUSITIS/OBI  
 L32 2601 SEA FILE-CAPLUS ABB-ON EMPHYSEMA/OBI  
 L33 6378 SEA FILE-CAPLUS ABB-ON FIBROSING/OBI (L) ALVEOLITIS/OBI OR

19

(PULMONARY/OBI OR LUNG/OBI OR RESPIRATORY/OBI) (L) (FIBROSIS/OBI  
 OR SARCOIDOSIS/OBI)  
 L34 6 SEA FILE-CAPLUS ABB-ON SLEEP DISORDERS/CT (L) RESPIRATORY/OBI  
 L35 943 SEA FILE-CAPLUS ABB-ON SLEEP/OBI (L) APNEA/OBI  
 L36 1691 SEA FILE-CAPLUS ABB-ON SARCOIDOSIS/CT  
 L37 39125 SEA FILE-CAPLUS ABB-ON DRUG INTERACTIONS-OLD, NT/CT  
 L38 4450 SEA FILE-CAPLUS ABB-ON DRUG DELIVERY SYSTEMS-OLD/CT (L) COMB?/OB  
 I  
 L39 16989 SEA FILE-CAPLUS ABB-ON COMBINATION CHEMOTHERAPY/CT  
 L40 5480 SEA FILE-CAPLUS ABB-ON COMB?/OBI (L) PHARMAC?/OBI  
 L41 6 SEA FILE-CAPLUS ABB-ON (L12 OR L19) AND (L13 OR L18) AND (L21  
 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30  
 OR L31 OR L32 OR L33 OR L34 OR L35 OR L36) AND (L37 OR L38 OR  
 L39 OR L40)  
 L5 1 SEA FILE-REGISTRY ABB-ON MORPHINE/CN  
 L6 1 SEA FILE-REGISTRY ABB-ON FENTANYL/CN  
 L7 1 SEA FILE-REGISTRY ABB-ON SUFENTANYL/CN  
 L8 1 SEA FILE-REGISTRY ABB-ON ALFENTANYL/CN  
 L9 1 SEA FILE-REGISTRY ABB-ON OXYMORPHONE/CN  
 L10 1 SEA FILE-REGISTRY ABB-ON HYDROMORPHONE/CN  
 L11 1 SEA FILE-REGISTRY ABB-ON OXYCODONE/CN  
 L12 31087 SEA FILE-CAPLUS ABB-ON (L5 OR L6 OR L7 OR L8 OR L9 OR L10)  
 L13 1073 SEA FILE-CAPLUS ABB-ON L11  
 L14 12914 SEA FILE-CAPLUS ABB-ON OPIOIDS/CT  
 L15 1209 SEA FILE-CAPLUS ABB-ON L14(L) KAPPA/OBI  
 L16 1944 SEA FILE-CAPLUS ABB-ON L14(L) MU/OBI  
 L17 56591 SEA FILE-CAPLUS ABB-ON AGONISTS/OBI  
 L18 368 SEA FILE-CAPLUS ABB-ON L15(L) L17  
 L19 454 SEA FILE-CAPLUS ABB-ON L15(L) L17  
 L20 19117 SEA FILE-CAPLUS ABB-ON RESPIRATORY TRACT/OBI  
 L21 76 SEA FILE-CAPLUS ABB-ON L20(L) CARCINOMA/OBI  
 L22 25232 SEA FILE-CAPLUS ABB-ON ASTHMA/OBI  
 L23 424 SEA FILE-CAPLUS ABB-ON BRONCHITIS/OBI OR BRONCHI?/OBI (L) DI  
 LATATION/OBI OR KARTAGENER/OBI  
 L24 28786 SEA FILE-CAPLUS ABB-ON TUBERCULOSIS/OBI  
 L25 4089 SEA FILE-CAPLUS ABB-ON BRONCHITIS/OBI  
 L26 120 SEA FILE-CAPLUS ABB-ON RESPIRATORY SYSTEM, NEOPLASM/CT  
 L27 35560 SEA FILE-CAPLUS ABB-ON LUNG, NEOPLASM/CT  
 L28 4982 SEA FILE-CAPLUS ABB-ON CHRONIC OBSTRUCTIVE PULMONARY/OBI OR  
 COPD/OBI  
 L29 7726 SEA FILE-CAPLUS ABB-ON BRONCHOPNEUMONIA/OBI OR PNEUMONIA/OBI  
 L30 136 SEA FILE-CAPLUS ABB-ON LARYNGITIS/OBI  
 L31 1101 SEA FILE-CAPLUS ABB-ON SINUSITIS/OBI  
 L32 2601 SEA FILE-CAPLUS ABB-ON EMPHYSEMA/OBI  
 L33 6378 SEA FILE-CAPLUS ABB-ON FIBROSING/OBI (L) ALVEOLITIS/OBI OR  
 (PULMONARY/OBI OR LUNG/OBI OR RESPIRATORY/OBI) (L) (FIBROSIS/OBI  
 OR SARCOIDOSIS/OBI)  
 L34 6 SEA FILE-CAPLUS ABB-ON SLEEP DISORDERS/CT (L) RESPIRATORY/OBI  
 L35 943 SEA FILE-CAPLUS ABB-ON SLEEP/OBI (L) APNEA/OBI  
 L36 1691 SEA FILE-CAPLUS ABB-ON SARCOIDOSIS/CT  
 L42 552 SEA FILE-CAPLUS ABB-ON (L12 OR L19) (L) (COMB?/OBI OR COADMIN?/O  
 BI OR CODRUGS/OBI OR CONCOMITANT?/OBI OR CONCURRENT?/OBI OR  
 BLEND?/OBI OR MIXTURES/OBI)  
 L43 82 SEA FILE-CAPLUS ABB-ON (L13 OR L18) (L) (COMB?/OBI OR COADMIN?/O  
 BI OR CODRUGS/OBI OR CONCOMITANT?/OBI OR CONCURRENT?/OBI OR  
 BLEND?/OBI OR MIXTURES/OBI)  
 L44 3 SEA FILE-CAPLUS ABB-ON L42 AND L43 AND (L21 OR L22 OR L23 OR

20

L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR  
L33 OR L34 OR L35 OR L36)

=> # 141,144 not 1210

L213 5 (L41 OR L44) NOT L210

=> fil embase; d que 182; d que 184

FILE 'EMBASE' ENTERED AT 11:12:33 ON 14 DEC 2006  
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FILE COVERS 1974 TO 13 DEC 2006 (20061213/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default)  
and biweekly.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

L48 53452 SEA FILE-EMBASE ABB-ON MORPHINE/CT  
L49 26736 SEA FILE-EMBASE ABB-ON FENTANYL/CT OR FENTANYL CITRATE/CT  
L50 4395 SEA FILE-EMBASE ABB-ON SUFENTANIL/CT OR SUFENTANIL CITRATE/CT

L51 4482 SEA FILE-EMBASE ABB-ON ALFENTANIL/CT  
L52 805 SEA FILE-EMBASE ABB-ON OXYMORPHONE/CT  
L53 2957 SEA FILE-EMBASE ABB-ON HYDROMORPHONE/CT  
L54 3754 SEA FILE-EMBASE ABB-ON OXYCODONE/CT  
L55 84233 SEA FILE-EMBASE ABB-ON ASTHMA-NT/CT  
L56 4535 SEA FILE-EMBASE ABB-ON BRONCHIECTASIS-NT/CT  
L57 15140 SEA FILE-EMBASE ABB-ON LUNG TUBERCULOSIS/CT  
L58 26377 SEA FILE-EMBASE ABB-ON CHRONIC OBSTRUCTIVE LUNG DISEASE/CT  
L59 22047 SEA FILE-EMBASE ABB-ON BRONCHITIS-NT/CT  
L60 2275 SEA FILE-EMBASE ABB-ON BRONCHOPNEUMONIA/CT  
L61 2500 SEA FILE-EMBASE ABB-ON LARYNGITIS-NT/CT  
L62 12991 SEA FILE-EMBASE ABB-ON SINUSITIS-NT/CT  
L63 13249 SEA FILE-EMBASE ABB-ON EMPHYSEMA-NT/CT  
L64 2738 SEA FILE-EMBASE ABB-ON FIBROSING ALVEOLITIS/CT  
L65 19527 SEA FILE-EMBASE ABB-ON LUNG FIBROSIS-NT/CT  
L66 11397 SEA FILE-EMBASE ABB-ON SARCOIDOSIS/CT  
L67 91685 SEA FILE-EMBASE ABB-ON LUNG CANCER-NT/CT  
L68 11977 SEA FILE-EMBASE ABB-ON SLEEP APNEA SYNDROME/CT  
L75 38068 SEA FILE-EMBASE ABB-ON DRUG POTENTIATION/CT  
L76 12328 SEA FILE-EMBASE ABB-ON MU OPIATE RECEPTOR AGONIST/CT  
L77 949 SEA FILE-EMBASE ABB-ON KAPPA OPIATE RECEPTOR AGONIST/CT  
L82 0 SEA FILE-EMBASE ABB-ON (L48 OR L49 OR L50 OR L51 OR L52 OR  
L53 OR L76) AND (L77 OR L54) AND L75 AND (L55 OR L56 OR L57 OR  
L58 OR L59 OR L60 OR L61 OR L62 OR L63 OR L64 OR L65 OR L66 OR  
L67 OR L68)

L48 53452 SEA FILE-EMBASE ABB-ON MORPHINE/CT  
L49 26736 SEA FILE-EMBASE ABB-ON FENTANYL/CT OR FENTANYL CITRATE/CT  
L50 4395 SEA FILE-EMBASE ABB-ON SUFENTANIL/CT OR SUFENTANIL CITRATE/CT

L51 4482 SEA FILE-EMBASE ABB-ON ALFENTANIL/CT  
L52 805 SEA FILE-EMBASE ABB-ON OXYMORPHONE/CT

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L53 2957 SEA FILE-EMBASE ABB-ON HYDROMORPHONE/CT  
L54 3754 SEA FILE-EMBASE ABB-ON OXYCODONE/CT  
L55 84233 SEA FILE-EMBASE ABB-ON ASTHMA-NT/CT  
L56 4535 SEA FILE-EMBASE ABB-ON BRONCHIECTASIS-NT/CT  
L57 15140 SEA FILE-EMBASE ABB-ON LUNG TUBERCULOSIS/CT  
L58 26377 SEA FILE-EMBASE ABB-ON CHRONIC OBSTRUCTIVE LUNG DISEASE/CT  
L59 22047 SEA FILE-EMBASE ABB-ON BRONCHITIS-NT/CT  
L60 2275 SEA FILE-EMBASE ABB-ON BRONCHOPNEUMONIA/CT  
L61 2500 SEA FILE-EMBASE ABB-ON LARYNGITIS-NT/CT  
L62 12991 SEA FILE-EMBASE ABB-ON SINUSITIS-NT/CT  
L63 13249 SEA FILE-EMBASE ABB-ON EMPHYSEMA-NT/CT  
L64 2738 SEA FILE-EMBASE ABB-ON FIBROSING ALVEOLITIS/CT  
L65 19527 SEA FILE-EMBASE ABB-ON LUNG FIBROSIS-NT/CT  
L66 11397 SEA FILE-EMBASE ABB-ON SARCOIDOSIS/CT  
L67 91685 SEA FILE-EMBASE ABB-ON LUNG CANCER-NT/CT  
L68 11977 SEA FILE-EMBASE ABB-ON SLEEP APNEA SYNDROME/CT  
L72 493 SEA FILE-EMBASE ABB-ON L54 (L) CB OR IT/CT CB-DRUG COMBINATIONS  
L76 12328 SEA FILE-EMBASE ABB-ON MU OPIATE RECEPTOR AGONIST/CT  
L77 949 SEA FILE-EMBASE ABB-ON KAPPA OPIATE RECEPTOR AGONIST/CT  
L78 208 SEA FILE-EMBASE ABB-ON L76 (L) CB OR IT/CT IT-DRUG INTERACTIONS  
L79 149 SEA FILE-EMBASE ABB-ON L77 (L) CB OR IT/CT  
L80 10397 SEA FILE-EMBASE ABB-ON (L48 OR L49 OR L50 OR L51 OR L52 OR  
L53) (L) CB OR IT/CT

L84 2 SEA FILE-EMBASE ABB-ON (L72 OR L79) AND (L80 OR L78) AND (L55  
OR L56 OR L57 OR L58 OR L59 OR L60 OR L61 OR L62 OR L63 OR L64  
OR L65 OR L66 OR L67 OR L68)

=> # 184 not 181

L214 2 L84 NOT L81

=> fil drugu; d que 1107

FILE 'DRUGU' ENTERED AT 11:12:35 ON 14 DEC 2006  
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FILE LAST UPDATED: 11 DEC 2006 <20061211/UP>  
DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<  
>>> THESAURUS AVAILABLE IN /CT <<<

L5 1 SEA FILE-REGISTRY ABB-ON MORPHINE/CN  
L6 1 SEA FILE-REGISTRY ABB-ON FENTANYL/CN  
L7 1 SEA FILE-REGISTRY ABB-ON SUFENTANIL/CN  
L8 1 SEA FILE-REGISTRY ABB-ON ALFENTANIL/CN  
L9 1 SEA FILE-REGISTRY ABB-ON OXYMORPHONE/CN  
L10 1 SEA FILE-REGISTRY ABB-ON HYDROMORPHONE/CN  
L11 1 SEA FILE-REGISTRY ABB-ON OXYCODONE/CN  
L87 9457 SEA FILE-DRUGU ABB-ON (L5 OR L6 OR L7 OR L8 OR L9 OR L10)  
L88 269 SEA FILE-DRUGU ABB-ON L11  
L89 19705 SEA FILE-DRUGU ABB-ON MORPHINE/CT  
L90 11240 SEA FILE-DRUGU ABB-ON FENTANYL/CT  
L91 2280 SEA FILE-DRUGU ABB-ON SUFENTANIL/CT  
L92 2680 SEA FILE-DRUGU ABB-ON ALFENTANIL/CT  
L93 252 SEA FILE-DRUGU ABB-ON OXYMORPHONE/CT  
L94 866 SEA FILE-DRUGU ABB-ON HYDROMORPHONE/CT

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L95 986 SEA FILE-DRUGU ABB-ON OXYCODONE/CT  
L97 125676 SEA FILE-DRUGU ABB-ON COMB./CT  
L98 43301 SEA FILE-DRUGU ABB-ON DRUG INTERACTIONS/CC  
L100 31287 SEA FILE-DRUGU ABB-ON ASTHMA OR BRONCHIECTASIS OR BRONCHI? (2A)  
DILATATION OR KARTAGENER OR TUBERCULOSIS  
L101 3808 SEA FILE-DRUGU ABB-ON COPD OR CHRONIC OBSTRUCTIVE (M) (LUNG OR  
PULMONARY OR RESPIRATORY)  
L102 24212 SEA FILE-DRUGU ABB-ON BRONCHITIS OR BRONCHOPNEUMONIA OR  
PNEUMONIA OR LARYNGITIS OR SINUSITIS OR EMPHYSEMA  
L103 1971 SEA FILE-DRUGU ABB-ON FIBROSING ALVEOLITIS OR FIBROSIS (A) (LUNG  
OR PULMONARY OR RESPIRATORY)  
L104 951 SEA FILE-DRUGU ABB-ON SARCOIDOSIS  
L105 17785 SEA FILE-DRUGU ABB-ON (LUNG OR PULMONARY OR RESPIRATORY) (2A) (C  
ANCERS OR NEOPLAS? OR CARCINOMAS)  
L106 433 SEA FILE-DRUGU ABB-ON SLEEP APNEA  
L107 4 SEA FILE-DRUGU ABB-ON (L97 OR L98) AND (L87 OR L89 OR L90 OR  
L91 OR L92 OR L93 OR L94) AND (L88 OR L95) AND (L100 OR L101  
OR L102 OR L103 OR L104 OR L105 OR L106)

=> # 1107 not 196

L215 4 L107 NOT L96

=> fil wpi; d que 1134; d que 1142

FILE 'WPIX' ENTERED AT 11:12:38 ON 14 DEC 2006  
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FILE LAST UPDATED: 8 DEC 2006 <20061208/UP>  
MOST RECENT THOMSON SCIENTIFIC UPDATE: 200679 <200679/DW>  
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> YOU ARE IN THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX <<<

>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX  
PLEASE VISIT:  
[http://www.stn-international.de/stndatabases/details/dwpi\\_r.html](http://www.stn-international.de/stndatabases/details/dwpi_r.html) <<<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,  
PLEASE VISIT:  
[http://www.stn-international.de/training-center/patents/stn\\_guide.pdf](http://www.stn-international.de/training-center/patents/stn_guide.pdf)

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE  
<http://scientific.thomson.com/support/patents/coverage/latestupdates/>

PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE  
[http://www.stn-international.de/stndatabases/details/ipc\\_reform.html](http://www.stn-international.de/stndatabases/details/ipc_reform.html) and  
<http://scientific.thomson.com/media/scpd/ipcdwpi.pdf>

>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX  
PLEASE SEE  
[http://www.stn-international.de/stndatabases/details/dwpi\\_r.html](http://www.stn-international.de/stndatabases/details/dwpi_r.html) <<<

>>> YOU ARE IN THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX <<<  
'BI ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

L117 198 SEA FILE-WPIX ABB-ON MU OPIOIDS/BI, ABEX  
L118 186 SEA FILE-WPIX ABB-ON KAPPA/BI, ABEX (1M) OPIOIDS/BI, ABEX  
L119 12146 SEA FILE-WPIX ABB-ON B14-L01/MC OR C14-L01/MC -AGONISTS  
L120 100 SEA FILE-WPIX ABB-ON L117(2A)AGONISTS/BI, ABEX OR (L117 AND  
L119)  
L121 102 SEA FILE-WPIX ABB-ON L118(2A)AGONISTS/BI, ABEX OR (L118 AND  
L119)  
L122 486502 SEA FILE-WPIX ABB-ON (M782 OR P867)/M0, M1, M2, M3, M4, M5, M6 OR  
A61K045/IPC OR (B12-C09 OR C12-C09 OR B14-S09 OR C14-S09)/MC  
L124 28604 SEA FILE-WPIX ABB-ON ASTHMA/BI, ABEX OR BRONCHIECTASIS/BI, ABEX  
OR BRONCHI?/BI, ABEX (2A) DILATATION/BI, ABEX OR KARTAGENER/BI, ABEX  
OR TUBERCULOSIS/BI, ABEX  
L125 5007 SEA FILE-WPIX ABB-ON COPD/BI, ABEX OR CHRONIC OBSTRUCTIVE/BI, AB  
EX (M) (LUNG/BI, ABEX OR PULMONARY/BI, ABEX OR RESPIRATORY/BI, ABEX)  
L126 11360 SEA FILE-WPIX ABB-ON BRONCHITIS/BI, ABEX OR BRONCHOPNEUMONIA/BI  
ABEX OR PNEUMONIA/BI, ABEX OR LARYNGITIS/BI, ABEX OR SINUSITIS/B  
I, ABEX OR EMPHYSEMA/BI, ABEX  
L127 2462 SEA FILE-WPIX ABB-ON FIBROSING ALVEOLITIS/BI, ABEX OR FIBROSIS/  
BI, ABEX (A) (LUNG/BI, ABEX OR PULMONARY/BI, ABEX OR RESPIRATORY/BI, AB  
EX)  
L128 3624 SEA FILE-WPIX ABB-ON SARCOIDOSIS/BI, ABEX OR SLEEP APNEA/BI, AB  
EX  
L129 8806 SEA FILE-WPIX ABB-ON (LUNG/BI, ABEX OR PULMONARY/BI, ABEX OR  
RESPIRATORY/BI, ABEX) (2A) (CANCER/BI, ABEX OR NEOPLAS?/BI, ABEX  
OR CARCINOMA/BI, ABEX)  
L134 1 SEA FILE-WPIX ABB-ON L120 AND L121 AND L122 AND (L124 OR L125  
OR L126 OR L127 OR L128 OR L129)  
L111 3147 SEA FILE-WPIX ABB-ON MORPHINE/BI, ABEX OR FENTANYL/BI, ABEX OR  
ALFENTANIL/BI, ABEX OR SUFENTANIL/BI, ABEX OR OXYMORPHONE/BI, ABEX  
OR MRZ2593/BI, ABEX OR MRZ 2593/BI, ABEX OR HYDROMORPHONE/BI, ABEX  
X  
L116 513 SEA FILE-WPIX ABB-ON OXYCODONE/BI, ABEX  
L117 198 SEA FILE-WPIX ABB-ON MU OPIOIDS/BI, ABEX  
L118 186 SEA FILE-WPIX ABB-ON KAPPA/BI, ABEX (1M) OPIOIDS/BI, ABEX  
L124 28604 SEA FILE-WPIX ABB-ON ASTHMA/BI, ABEX OR BRONCHIECTASIS/BI, ABEX  
OR BRONCHI?/BI, ABEX (2A) DILATATION/BI, ABEX OR KARTAGENER/BI, ABEX  
OR TUBERCULOSIS/BI, ABEX  
L125 5007 SEA FILE-WPIX ABB-ON COPD/BI, ABEX OR CHRONIC OBSTRUCTIVE/BI, AB  
EX (M) (LUNG/BI, ABEX OR PULMONARY/BI, ABEX OR RESPIRATORY/BI, ABEX)  
L126 11360 SEA FILE-WPIX ABB-ON BRONCHITIS/BI, ABEX OR BRONCHOPNEUMONIA/BI  
ABEX OR PNEUMONIA/BI, ABEX OR LARYNGITIS/BI, ABEX OR SINUSITIS/B  
I, ABEX OR EMPHYSEMA/BI, ABEX  
L127 2462 SEA FILE-WPIX ABB-ON FIBROSING ALVEOLITIS/BI, ABEX OR FIBROSIS/  
BI, ABEX (A) (LUNG/BI, ABEX OR PULMONARY/BI, ABEX OR RESPIRATORY/BI, AB  
EX)  
L128 3624 SEA FILE-WPIX ABB-ON SARCOIDOSIS/BI, ABEX OR SLEEP APNEA/BI, AB  
EX  
L129 8806 SEA FILE-WPIX ABB-ON (LUNG/BI, ABEX OR PULMONARY/BI, ABEX OR  
RESPIRATORY/BI, ABEX) (2A) (CANCER/BI, ABEX OR NEOPLAS?/BI, ABEX  
OR CARCINOMA/BI, ABEX)  
L138 84 SEA FILE-WPIX ABB-ON L118(2A)AGONISTS/BI, ABEX  
L139 61 SEA FILE-WPIX ABB-ON L117(2A)AGONISTS/BI, ABEX  
L140 384 SEA FILE-WPIX ABB-ON ((L111 OR L139) (5A)) ((L116 OR L138))  
L141 10 SEA FILE-WPIX ABB-ON L140(5A) (COMB?/BI, ABEX OR CODRUG?/BI, ABEX

OR COADMIN?/BI.ABEX OR COCOMITANT?/BI.ABEX OR CONCURRENT?/BI.  
ABEX OR BLEND?/BI.ABEX OR MIX?/BI.ABEX  
L142 2 SEA FILE=WPX ABX-ON L141 AND (L124 OR L125 OR L126 OR L127  
OR L128 OR L129)

=> a l134,l142 not l211

L216 2 (L134 OR L142) NOT L211

=> fil medl; d que l189; d que l197; d que l207; d que l179

FILE 'MEDLINE' ENTERED AT 11:12:43 ON 14 DEC 2006

FILE LAST UPDATED: 13 Dec 2006 (20061213/UP). FILE COVERS 1950 TO DATE.

In preparation for the annual MEDLINE reload, the National Library of  
Medicine (NLM) has suspended delivery of regular updates as of November  
15, 2006. In-process and in-data-review records will resume delivery  
on November 21, 2006, and will continue to be added to MEDLINE until  
December 17, 2006.

On December 17, 2006, all regular MEDLINE updates from November 15 to  
December 16 will be added to MEDLINE, along with 2007 Medical Subject  
Headings (MeSH(R)) and 2007 tree numbers.

The annual reload will be available in early 2007.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

L180( 28104)SEA FILE=MEDLINE ABX-ON MORPHINE/CT  
L181( 10382)SEA FILE=MEDLINE ABX-ON FENTANYL-NT/CT  
L182( 294)SEA FILE=MEDLINE ABX-ON OXYMORPHONE/CT  
L183( 704)SEA FILE=MEDLINE ABX-ON HYDROMORPHONE/CT  
L184( 540)SEA FILE=MEDLINE ABX-ON OXYCODONE/CT  
L185( 108974)SEA FILE=MEDLINE ABX-ON DRUG INTERACTIONS-NT/CT  
L186( 42787)SEA FILE=MEDLINE ABX-ON DRUG COMBINATIONS/CT  
L187( 97253)SEA FILE=MEDLINE ABX-ON DRUG THERAPY, COMBINATION/CT  
L188( 15)SEA FILE=MEDLINE ABX-ON (L180 OR L181 OR L182 OR L183) AND  
L184 AND (L185 OR L186 OR L187)  
L189 3 SEA FILE=MEDLINE ABX-ON L188 AND SYNERG7

L190( 108974)SEA FILE=MEDLINE ABX-ON DRUG INTERACTIONS-NT/CT  
L191( 42787)SEA FILE=MEDLINE ABX-ON DRUG COMBINATIONS/CT  
L192( 97253)SEA FILE=MEDLINE ABX-ON DRUG THERAPY, COMBINATION/CT  
L193( 1136)SEA FILE=MEDLINE ABX-ON RECEPTORS, OPIOID, MU/CT(L)AG/CT  
L194( 881)SEA FILE=MEDLINE ABX-ON RECEPTORS, OPIOID, KAPPA/CT(L)AG/CT  
L195( 23)SEA FILE=MEDLINE ABX-ON L193 AND L194 AND (L190 OR L191 OR  
L192)  
L196( 240557)SEA FILE=MEDLINE ABX-ON DOSE-RESPONSE RELATIONSHIP, DRUG/CT  
L197 1 SEA FILE=MEDLINE ABX-ON L195 AND L196 AND CONDITIONING,  
OPERANT/CT

L198( 28104)SEA FILE=MEDLINE ABX-ON MORPHINE/CT  
L199( 10382)SEA FILE=MEDLINE ABX-ON FENTANYL-NT/CT  
L200( 294)SEA FILE=MEDLINE ABX-ON OXYMORPHONE/CT  
L201( 704)SEA FILE=MEDLINE ABX-ON HYDROMORPHONE/CT  
L202( 540)SEA FILE=MEDLINE ABX-ON OXYCODONE/CT  
L203( 1136)SEA FILE=MEDLINE ABX-ON RECEPTORS, OPIOID, MU/CT(L)AG/CT  
L204( 881)SEA FILE=MEDLINE ABX-ON RECEPTORS, OPIOID, KAPPA/CT(L)AG/CT  
L205( 488)SEA FILE=MEDLINE ABX-ON (L198 OR L199 OR L200 OR L201 OR  
L203) AND (L202 OR L204)  
L206( 8267)SEA FILE=MEDLINE ABX-ON COUGH/CT  
L207 1 SEA FILE=MEDLINE ABX-ON L205 AND L206

L164( 28104)SEA FILE=MEDLINE ABX-ON MORPHINE/CT  
L165( 10382)SEA FILE=MEDLINE ABX-ON FENTANYL-NT/CT  
L166( 294)SEA FILE=MEDLINE ABX-ON OXYMORPHONE/CT  
L167( 704)SEA FILE=MEDLINE ABX-ON HYDROMORPHONE/CT  
L168( 540)SEA FILE=MEDLINE ABX-ON OXYCODONE/CT  
L169( 124991)SEA FILE=MEDLINE ABX-ON LUNG DISEASES, OBSTRUCTIVE-NT/CT  
L170( 5936)SEA FILE=MEDLINE ABX-ON BRONCHITIS-NT/CT  
L171( 57086)SEA FILE=MEDLINE ABX-ON TUBERCULOSIS, PULMONARY-NT/CT  
L172( 3460)SEA FILE=MEDLINE ABX-ON BRONCHOPNEUMONIA/CT  
L173( 3610)SEA FILE=MEDLINE ABX-ON LARYNGITIS-NT/CT  
L174( 11628)SEA FILE=MEDLINE ABX-ON SINUSITIS-NT/CT  
L175( 13172)SEA FILE=MEDLINE ABX-ON PULMONARY FIBROSIS/CT  
L176( 1561)SEA FILE=MEDLINE ABX-ON SARCOIDOSIS, PULMONARY/CT  
L177( 113814)SEA FILE=MEDLINE ABX-ON LUNG NEOPLASMS-NT/CT  
L178( 12706)SEA FILE=MEDLINE ABX-ON SLEEP APNEA SYNDROMES-NT/CT  
L179 1 SEA FILE=MEDLINE ABX-ON (L164 OR L165 OR L166 OR L167) AND  
L168 AND (L169 OR L170 OR L171 OR L172 OR L173 OR L174 OR L175  
OR L176 OR L177 OR L178)

=> a l189,l197,l207,l179

L217 6 (L189 OR L197 OR L207 OR L179)

=> > dup rem l217,l215,l213,l216,l214

FILE 'MEDLINE' ENTERED AT 11:13:15 ON 14 DEC 2006

FILE 'DRUGS' ENTERED AT 11:13:15 ON 14 DEC 2006

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FILE 'CAPLUS' ENTERED AT 11:13:15 ON 14 DEC 2006

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FILE 'EMBASE' ENTERED AT 11:13:15 ON 14 DEC 2006

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PROCESSING COMPLETED FOR L217

PROCESSING COMPLETED FOR L215

PROCESSING COMPLETED FOR L213

PROCESSING COMPLETED FOR L216

PROCESSING COMPLETED FOR L214

L218 19 DUP REM L217 L215 L213 L216 L214 (0 DUPLICATES REMOVED)

ANSWERS '1-6' FROM FILE MEDLINE  
ANSWERS '7-10' FROM FILE DRUGS  
ANSWERS '11-15' FROM FILE CAPLUS  
ANSWERS '16-17' FROM FILE WPX  
ANSWERS '18-19' FROM FILE EMBASE

=> d iall 1-10; d ibib ed abe hit 11-15; d ibib abeq tech hitser 16-17; d iall 18-  
19; fil hom

L218 ANSWER 1 OF 19 MEDLINE on STN  
ACCESSION NUMBER: 2006205320 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 16612168  
TITLE: Efficacy of controlled-release oxycodone for dyspnea in  
cancer patients: three case series.  
AUTHOR: Shinjo Takuya; Okada Masakuni  
CORPORATE SOURCE: Dept. of Palliative Care Unit, Shikaihoken Kobe Central  
Hospital.  
SOURCE: Gan to kagaku ryoho. Cancer & chemotherapy, (2006 Apr) Vol.  
33, No. 4, pp. 529-32.  
Journal code: 7810034. ISSN: 0385-0684.  
PUB. COUNTRY: Japan  
DOCUMENT TYPE: (CASE REPORTS)  
JOURNAL: Article; (JOURNAL ARTICLE)  
LANGUAGE: Japanese  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200605  
ENTRY DATE: Entered STN: 14 Apr 2006  
Last Updated on STN: 10 May 2006  
Entered Medline: 9 May 2006

ABSTRACT:  
Dyspnea is a common symptom in patients with advanced cancer. Systemic  
morphine administration has been reported as an effective pharmacological  
treatment to control dyspnea. However, there have been few reports on similar  
effects of alternative opioids except for morphine. To evaluate the effect of  
controlled-release oxycodone on the relief of dyspnea, we investigated three  
cases with opioid substitution from subcutaneous morphine to oral oxycodone.  
In all cases, both opioids provided equivalent effects for the palliation of  
cancer dyspnea with no significant adverse effects. Future studies in the  
appropriate clinical designs will be needed to confirm our findings.

CONTROLLED TERM: Check Tags: Female: Male  
Administration, Oral  
Aged  
\*Analgesics, Opioid: AD, administration & dosage  
Delayed-Action Preparations  
\*Dyspnea: DT, drug therapy  
Dyspnea: ET, etiology  
English Abstract  
Humans  
Injections, Subcutaneous  
Lung Neoplasms: CO, complications  
Lung Neoplasms: PP, physiopathology  
Middle Aged  
Morphine: AD, administration & dosage  
\*Oxycodone: AD, administration & dosage  
CAS REGISTRY NO.: 57-27-2 (Morphine); 76-42-6 (Oxycodone)  
CHEMICAL NAME: 0 (Analgesics, Opioid); 0 (Delayed-Action Preparations)

L218 ANSWER 2 OF 19 MEDLINE on STN  
ACCESSION NUMBER: 2005170367 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 15801946

TITLE: Co-administration of oxycodone and morphine and analgesic  
synergy re-examined.  
AUTHOR: Smith Mace T; de la Iglesia Felix A  
SOURCE: British journal of clinical pharmacology, (2005 Apr) Vol.  
59, No. 4, pp. 486-7; author reply 487-8.  
Journal code: 7503323. ISSN: 0306-5251.  
COMMENT: Comment on: Br J Clin Pharmacol. 2004 Sep;58(3):235-42.  
PubMed ID: 15327582  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Commentary  
Letter  
English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200508  
ENTRY DATE: Entered STN: 2 Apr 2005  
Last Updated on STN: 2 Aug 2005  
Entered Medline: 1 Aug 2005  
CONTROLLED TERM: \*Analgesics, Opioid: AD, administration & dosage  
\*Cold  
Drug Combinations  
Drug Synergism  
Humans  
\*Morphine: AD, administration & dosage  
\*Nociceptors: DE, drug effects  
\*Oxycodone: AD, administration & dosage  
\*Pain: PC, prevention & control  
CAS REGISTRY NO.: 57-27-2 (Morphine); 76-42-6 (Oxycodone)  
CHEMICAL NAME: 0 (Analgesics, Opioid); 0 (Drug Combinations)

L218 ANSWER 3 OF 19 MEDLINE on STN  
ACCESSION NUMBER: 2004422001 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 15327582  
TITLE: Can coadministration of oxycodone and morphine produce  
analgesic synergy in humans? An experimental cold  
pain study.  
AUTHOR: Grach Michael; Massalha Wattan; Pud Dorit; Adler Rivka;  
Eisenberg Elon  
CORPORATE SOURCE: Department of Anaesthesiology, Carmel Hospital, Haifa,  
Israel.  
SOURCE: British journal of clinical pharmacology, (2004 Sep) Vol.  
58, No. 3, pp. 235-42.  
Journal code: 7503323. ISSN: 0306-5251.  
COMMENT: Comment in: Br J Clin Pharmacol. 2005 Apr;59(4):486-7;  
author reply 487-8. PubMed ID: 15801946  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: (CLINICAL TRIAL)  
JOURNAL: Article; (JOURNAL ARTICLE)  
(RANDOMIZED CONTROLLED TRIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200412  
ENTRY DATE: Entered STN: 26 Aug 2004  
Last Updated on STN: 20 Dec 2004  
Entered Medline: 17 Dec 2004

ABSTRACT:  
AIMS: The coadministration of subantinociceptive doses of oxycodone with  
morphine has recently been shown to result in a synergistic  
antinociceptive effect in rats. The present study was aimed to investigate the  
possibility that coadministration of morphine and oxycodone can produce a  
similar synergistic effect in humans exposed to an experimental model

10/661458

of cold pressor test (CPT). METHODS: The enriched enrollment design was used to exclude 'stoic' and 'placebo responders' in a single-blind fashion. 'Monostic', placebo 'nonresponder' female volunteers (n = 30) were randomly assigned to receive 0.3 mg/kg(-1) oral morphine sulphate, 0.5 mg/kg(-1) oral oxycodone hydrochloride, and the combination of 0.25 mg/kg(-1) morphine sulphate with 0.25 mg/kg(-1) oxycodone hydrochloride, 1 week apart from each other, in a double-blind crossover design. Latency to pain onset (threshold), pain intensity (VAS), and pain tolerance (time until removal of the hand from the water) were measured six times over a 3-h period, subsequent to the administration of each medication, and were used to assess their antinociceptive effect. RESULTS: The combination produced a significantly higher effect on latency to pain onset than that of morphine alone [difference in mean postbaseline value 2.2; 95% confidence interval (CI) 0.48, 3.9; P = 0.01] but the effect was nonsignificantly smaller than that of oxycodone alone. Similarly, the effect of the combination on pain tolerance was significantly larger than that of morphine alone (combination difference 8.4; 95% CI 2.5, 14.3; P = 0.007), whereas oxycodone alone caused a nonsignificantly larger effect than that of the combination treatment. Comparisons of pain magnitude failed to show any significant differences between the three treatments. CONCLUSIONS: These results indicate that at the doses tested, morphine and oxycodone do not produce synergistic antinociceptive effects in healthy humans exposed to the CPT.

CONTROLLED TERM: Check Tags: Female

Adolescent  
Adult  
\*Analgesics, Opioid: AD, administration & dosage  
\*Cold  
Cross-Over Studies  
Double-Blind Method  
Drug Combinations  
Drug Synergism  
Humans  
\*Morphine: AD, administration & dosage  
\*Oxycodone: AD, administration & dosage  
\*Pain: PC, prevention & control  
Research Support, Non-U.S. Gov't  
57-27-2 (Morphine); 76-42-6 (Oxycodone)  
0 (Analgesics, Opioid); 0 (Drug Combinations)

CAS REGISTRY NO.:

CHEMICAL NAME:

L218 ANSWER 4 OF 19

ACCESSION NUMBER:

DOCUMENT NUMBER:

TITLE:

AUTHOR:

CORPORATE SOURCE:

CONTRACT NUMBER:

SOURCE:

PUB. COUNTRY:

DOCUMENT TYPE:

LANGUAGES:

MEDLINE on STN

2003060915 MEDLINE Full-text

PubMed ID: 14557380

Opioid interactions in rhesus monkeys: effects of delta + mu and delta + kappa agonists on schedule-controlled responding and thermal nociception.  
Stevenson Glenn W; Folk John E; Linsmeyer David C; Rice Kenner C; Negus S Stevens

Alcohol and Drug Abuse Research Center, Harvard Medical School, McLean Hospital, 115 Mill St., Belmont, MA 02478-9106, USA.

P01-DA14528 (NIDA)

R01-DA14460 (NIDA)

T32-DA07252 (NIDA)

The Journal of pharmacology and experimental therapeutics, (2003 Dec) Vol. 307, No. 3, pp. 1054-64. Electronic Publication: 2003-10-13.

Journal code: 0376362. ISSN: 0022-3565.

United States

Journal; Article; (JOURNAL ARTICLE)

English

29

10/661458

FILE SEGMENT:

ENTRY MONTH:

ENTRY DATE:

Priority Journals

200401

Entered STN: 24 Dec 2003

Last Updated on STN: 30 Jan 2004

Entered Medline: 29 Jan 2004

ABSTRACT:

Agonists at delta, mu, and kappa opioid receptors produce interacting effects in rodents and nonhuman primates. To further evaluate the determinants of these interactions, this study examined the effects of mixtures of delta + mu and delta + kappa agonists in rhesus monkeys (n = 4-5) using two behavioral procedures, an assay of schedule-controlled responding for food reinforcement and an assay of thermal nociception. Results were analyzed using dose-addition analysis. In the assay of schedule-controlled responding, the delta agonist (+)-4-[[alphaR]-alpha-(2S,5R)-4-allyl-2,5-dimethyl-1-piperazinyl]-3-methoxybenzyl]-N,N-diethylbenzamide (SNCR0); the mu agonists methadone, fentanyl, morphine, and nalbuphine; and the kappa agonists (alpha,7alpha,beta)-(-)-N-methyl-N-(7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl) benzeneacetamide (U69,593) and bremazocine all dose dependently decreased rates of food-maintained responding when administered alone. Fixed ratio mixtures of SNCR0 + mu agonists produced additive or subadditive effects, whereas SNCR0 + kappa agonist mixtures produced only additive effects. In the assay of thermal nociception, SNCR0 produced no measurable effects when administered alone, whereas mu and kappa agonists produced dose-dependent antinociception. SNCR0 + mu agonist mixtures produced superadditive effects manifested as leftward shifts in mu agonist dose-effect curves. This synergism was antagonized by the delta-selective antagonist naltrindole, suggesting that SNCR0-induced enhancement of mu agonist antinociception was delta receptor-mediated. SNCR0 did not enhance the antinociceptive effects of the highly selective kappa agonist U69,593, and it produced only a marginal enhancement of antinociception produced by the less selective kappa agonist bremazocine. These results suggest that delta agonists may selectively enhance the antinociceptive effects of mu agonists in rhesus monkeys. These results also confirm that opioid agonist interactions may depend on the receptor selectivity and relative doses of the agonists and on the experimental endpoint.

CONTROLLED TERM:

Check Tags: Male

\*Analgesics, Opioid: PD, pharmacology  
Animals  
Benzamides: PD, pharmacology  
Benzeneacetamides: PD, pharmacology  
Benzomorphans: PD, pharmacology  
\*Conditioning, Operant: DR, drug effects  
Dose-Response Relationship, Drug  
Drug Interactions  
Heat  
Macaca mulatta  
\*Naltrexone: AA, analogs & derivatives  
Naltrexone: PD, pharmacology  
Narcotic Antagonists: PD, pharmacology  
\*Pain: PX, psychology  
Piperazines: PD, pharmacology  
Pyrrolidines: PD, pharmacology  
\*Receptors, Opioid, delta: AG, agonists  
\*Receptors, Opioid, kappa: AG, agonists  
\*Receptors, Opioid, mu: AG, agonists  
Reinforcement Schedule  
Research Support, U.S. Gov't, P.H.S.  
11555-53-4 (naltrindole); 156727-74-1 (4-(alpha-(4-allyl-2,5-dimethyl-1-piperazinyl)-3-methoxybenzyl)-N,N-diethylbenzamide); 16590-41-3 (Naltrexone); 75684-07-0 (bremazocine); 96744-75-1 (U 69593)

CAS REGISTRY NO.:

10/661458

10/661458

CHEMICAL NAME: 0 (Analgesics, Opioid); 0 (Benzamides); 0 (Benzeneacetamides); 0 (Benzomorphans); 0 (Narcotic Antagonists); 0 (Piperazines); 0 (Pyrrolidines); 0 (Receptors, Opioid, delta); 0 (Receptors, Opioid, kappa); 0 (Receptors, Opioid, mu)

L218 ANSWER 5 OF 19

ACCESSION NUMBER:

DOCUMENT NUMBER:

TITLE:

AUTHOR:

CORPORATE SOURCE:

SOURCE:

PUB. COUNTRY:

DOCUMENT TYPE:

LANGUAGES:

FILE SEGMENT:

ENTRY MONTH:

ENTRY DATE:

MEDLINE on STN

2000107229 MEDLINE Full-text

PubMed ID: 10640321

The antitussive activity of delta-opioid receptor stimulation in guinea pigs.  
Kotzer C J; Hay D W; Dondio G; Giardina G; Petrillo P; Underwood D C

Department of Pulmonary Pharmacology, SmithKline Beecham Pharmaceuticals, King of Prussia, Pennsylvania, USA.

The Journal of pharmacology and experimental therapeutics, (2000 Feb) Vol. 292, No. 2, pp. 803-9.

Journal code: 0376362. ISSN: 0022-3565.

United States

Journal; Article; (JOURNAL ARTICLE)

English

Priority Journals

200002

Entered STN: 9 Mar 2000

Last Updated on STN: 9 Mar 2000

Entered Medline: 22 Feb 2000

ABSTRACT:

In this study, the activity of the delta-opioid receptor subtype-selective agonist, SB 271222, was investigated in a guinea pig model of citric acid-induced cough. Parenteral administration of selective agonists of the delta-opioid receptor (SB 271222), mu-opioid receptor (codeine and hydrocodone), and kappa-opioid receptor (BRL 52974) produced dose-related inhibition of citric acid-induced cough with ED(50) values of 7.3, 5.2, 5.1, and 5.3 mg/kg, respectively. The nonselective opioid receptor antagonist, naloxone (3 mg/kg, i.v.), attenuated the antitussive effects of codeine or SB 271222, indicating that the antitussive activity of both compounds is opioid receptor-mediated. The delta-receptor antagonist, SB 244525 (10 mg/kg, i.p.), inhibited the antitussive effect of SB 271222 (20 mg/kg, i.p.). In contrast, combined pretreatment with beta-maltrexamine (mu-receptor antagonist; 20 mg/kg, s.c.) and nalmeforphine (kappa-receptor antagonist; 20 mg/kg, s.c.), at doses that inhibited the antitussive activity of mu- and kappa-receptor agonists, respectively, was without effect on the antitussive response of SB 271222 (20 mg/kg, i.p.). The sigma-receptor antagonist rimcazole (3 mg/kg, i.p.) inhibited the antitussive effect of dextromethorphan (30 mg/kg, i.p.), a sigma-receptor agonist, but not that of SB 271222. These studies provide compelling evidence that the antitussive effects of SB 271222 in this guinea pig cough model are mediated by agonist activity at the delta-opioid receptor.

CONTROLLED TERM:

Check Tags: Male  
Animals  
CHO Cells  
Carbazoles: PD, pharmacology  
Cell Line  
Cloning, Organism  
Codeine: PD, pharmacology  
\*Cough: PC, prevention & control  
Crizotinae  
Dextromethorphan: PD, pharmacology  
Disease Models, Animal  
Dose-Response Relationship, Drug

Drug Interactions

Guinea Pigs

Humans

Hydrocodone: PD, pharmacology

\*Levallorphan: AA, analogs &amp; derivatives

Levallorphan: TU, therapeutic use

Naloxone: PD, pharmacology

\*Narcotic Antagonists: PD, pharmacology

Protein Binding

Pyridines: PD, pharmacology

\*Pyrroles: TU, therapeutic use

Pyrrolidines: PD, pharmacology

Receptors, Opioid, delta: AG, agonists

\*Receptors, Opioid, delta: DE, drug effects

\*Receptors, Opioid, delta: PH, physiology

Receptors, Opioid, kappa: AG, agonists

Receptors, Opioid, kappa: DE, drug effects

Receptors, Opioid, kappa: PH, physiology

Receptors, Opioid, mu: AG, agonists

Receptors, Opioid, mu: DE, drug effects

Receptors, Opioid, mu: PH, physiology

CAS REGISTRY NO.:

125-29-1 (Hydrocodone); 125-71-3 (Dextromethorphan); 15544-79-2 (BRL 52974); 152-02-3 (Levallorphan); 465-65-6 (Naloxone); 75589-04-0 (rimcazole); 76-57-3 (Codeine)  
0 (Carbazoles); 0 (Narcotic Antagonists); 0 (Pyridines); 0 (Pyrroles); 0 (Pyrrolidines); 0 (Receptors, Opioid, delta); 0 (Receptors, Opioid, kappa); 0 (Receptors, Opioid, mu); 0 (SB 271222)

L218 ANSWER 6 OF 19

ACCESSION NUMBER:

DOCUMENT NUMBER:

TITLE:

AUTHOR:

CORPORATE SOURCE:

SOURCE:

PUB. COUNTRY:

DOCUMENT TYPE:

LANGUAGES:

FILE SEGMENT:

ENTRY MONTH:

ENTRY DATE:

MEDLINE on STN

2000130083 MEDLINE Full-text

PubMed ID: 10666549

Co-administration of sub-antinociceptive doses of oxycodone and morphine produces marked antinociceptive synergy with reduced CNS side-effects in rats.

Ross P B; Wallis S C; Smith W T  
School of Pharmacy, The University of Queensland, St Lucia, Brisbane, Australia.

Pain, (2000 Feb) Vol. 84, No. 2-3, pp. 421-8.

Journal code: 7508666. ISSN: 0304-3959.

Netherlands

Journal; Article; (JOURNAL ARTICLE)

English

Priority Journals

200003

Entered STN: 27 Mar 2000

Last Updated on STN: 27 Mar 2000

Entered Medline: 16 Mar 2000

ABSTRACT:

Oxycodone and morphine are structurally related, strong opioid analgesics, commonly used to treat moderate to severe pain in humans. Although it is well-established that morphine is a mu-opioid agonist, this is not the case for oxycodone. Instead, our recent studies have shown that oxycodone appears to be a kappa-opioid agonist (Ross and Smith, 1997). In the current study, we now show that co-administration of sub-antinociceptive doses of oxycodone (putative kappa-opioid agonist) with morphine (mu-opioid agonist) to rats by both the intracerebroventricular and by systemic routes (intraperitoneal and subcutaneous), results in markedly increased (synergistic) levels of antinociception. Behaviourally, rats co-administered sub-antinociceptive doses of oxycodone and morphine were similar to control rats dosed with saline,

31

32



whereas rats that received equi-potent doses of either opioid alone, were markedly sedated. These results suggest that co-administration of sub-analgesic doses of oxycodone and morphine to patients may provide excellent pain relief with a reduction in opioid-related CNS side-effects. Controlled clinical trials in appropriate patient populations are required to evaluate this possibility. (1)

CONTROLLED TERM: Check Tags: Male  
 Analgesics, Opioid: AD, administration & dosage  
 Analgesics, Opioid: PD, pharmacology  
 Animals  
 Behavior, Animal: DR, drug effects  
 Central Nervous System: DR, drug effects  
 Dose-Response Relationship, Drug  
 Drug Combinations  
 Drug Synergism  
 Injections, Intraperitoneal  
 Injections, Intraventricular  
 Injections, Subcutaneous  
 Morphine: AD, administration & dosage  
 Morphine: PD, pharmacology  
 Nociceptors: DR, drug effects  
 Oxycodone: AD, administration & dosage  
 Oxycodone: PD, pharmacology  
 Rats  
 Rats, Sprague-Dawley  
 Research Support, Non-U.S. Gov't  
 CAS REGISTRY NO.: 57-27-2 (Morphine); 76-42-6 (Oxycodone)  
 CHEMICAL NAME: 0 (Analgesics, Opioid); 0 (Drug Combinations)

L218 ANSWER 7 OF 19 DRUGU COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 1995-21708 DRUGU T Full-text  
 TITLE: A pain syndrome associated with large adrenal masses in patients with lung cancer.  
 AUTHOR: Berger M S; Cooley M B; Abraham J L  
 CORPORATE SOURCE: Univ. Pennsylvania  
 LOCATION: Philadelphia, Pa., USA  
 SOURCE: J. Pain Symptom Manage. (10, No. 2, 161-66, 1995) 2 Fig. 13  
 Ref.  
 AVAIL. OF DOC.: Hematology-Oncology Division, Philadelphia VA Medical Center.  
 University and Woodlands Avenues, Philadelphia, PA, U.S.A.  
 LANGUAGE: English  
 DOCUMENT TYPE: Journal

## ABSTRACT:

Case histories are reported of 2 patients with lung cancer who had a pain syndrome caused by large adrenal metastases. Patient 1 had a poor response to radiation, controlled-release p.o. morphine and acetaminophen-oxycodone. He responded to chemotherapy with cyclophosphamide (Cytosan), Adriamycin and vincristine (CAV). He was given hydrocortisone for orthostatic hypotension. Hip pain developed and he died. Patient 2 was treated with controlled-release p.o. morphine until pain progressed and he died. 23 Previously recorded cases were reviewed.

SECTION HEADING: T Therapeutics

CLASSIF. CODE: 43 Analgesics, NSAIDs  
 44 Narcotics

CONTROLLED TERM: ADRENAL \*TR; METASTASIS \*TR; ADRENOPATHY \*TR; NEOPLASM \*TR; PAIN \*TR; LUNG \*OC; SMALL-CELL \*OC; LARGE-CELL \*OC; NEOPLASM \*OC; HYDROCORTISONE \*RC; CASE-HISTORY \*FT; IN-VIVO \*FT; RADIOTHERAPY \*FT; CONCOMITANT-DISEASE \*FT; EXITUS \*FT; CASES \*FT  
 [01] MORPHINE \*TR; MORPHINE \*RN; ANALGESIC \*FT; DEPOT \*FT; P.O. \*FT; PHARM.PREP. \*FT; ANALGESICS \*FT; NARCOTICS \*FT; SEDATIVES \*FT; 57-27-2 \*FT; TR \*FT  
 CAS REGISTRY NO.: 57-27-2  
 [02] OXYCODONE \*TR; OXYCODONE \*RN; COMB.PREP. \*FT; P.O. \*FT; ANALGESIC \*FT; ANALGESICS \*FT; NARCOTICS \*FT; SEDATIVES \*FT; 76-42-6 \*FT; TR \*FT  
 CAS REGISTRY NO.: 76-42-6  
 [03] PARACETAMOL \*TR; PARACETAM \*RN; COMB.PREP. \*FT; ANALGESIC \*FT; P.O. \*FT; ANALGESICS \*FT; ANTIPYRETICS \*FT; 103-90-2 \*FT; TR \*FT  
 CAS REGISTRY NO.: 103-90-2  
 [04] CYCLOPHOSPHAMIDE \*TR; CYTOXAN \*TR; CYCLOPHOS \*RN; CYTOSTATIC \*FT; CYTOSTATIC-COMB. \*FT; COMB. \*FT; CYTOSTATICS \*FT; IMMUNOSUPPRESSIVES \*FT; 50-18-0 \*FT; TR \*FT  
 CAS REGISTRY NO.: 50-18-0  
 [05] DOXORUBICIN \*TR; ADRIAMYCIN \*TR; DOXORUBIC \*RN; CYTOSTATIC \*FT; CYTOSTATIC-COMB. \*FT; COMB. \*FT; ANTIBIOTICS \*FT; CYTOSTATICS \*FT; 23214-92-8 \*FT; TR \*FT  
 CAS REGISTRY NO.: 23214-92-8  
 [06] VINCRISTINE \*TR; VINCRISTI \*RN; CYTOSTATIC \*FT; CYTOSTATIC-COMB. \*FT; COMB. \*FT; CYTOSTATICS \*FT; 57-22-7 \*FT; TR \*FT  
 CAS REGISTRY NO.: 57-22-7  
 FIELD AVAIL.: AB; LA; CT  
 FILE SEGMENT: Literature

L218 ANSWER 8 OF 19 DRUGU COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 1993-55507 DRUGU T S Full-text  
 TITLE: A Risk-Benefit Appraisal of Injectable NSAIDs in the Management of Postoperative Pain.  
 AUTHOR: Nuutinen L S; Laitinen J O; Salomaki T E  
 LOCATION: Kuopio, Oulu, Finland  
 SOURCE: Drug Safety (19, No. 5, 380-93, 1993) 3 Tab. 124 Ref.  
 ISSN: 0114-5916  
 AVAIL. OF DOC.: Department of Anaesthesiology, University Hospital, P.O.B 1777, SF-70211 Kuopio, Finland.  
 LANGUAGE: English  
 DOCUMENT TYPE: Journal

## ABSTRACT:

Injectable NSAIDs in the management of postoperative pain are reviewed, with reference to their mode of action, the use of indometacin (IN), diclofenac (DI), ketorolac (KE) and other NSAIDs for acute pain, the adverse effects of NSAIDs on the GI system, coagulation and renal and other adverse effects. Somnolence, dry mouth and GI effects are the commonest adverse events with KE. Interactions occur between NSAIDs and anticoagulants, diuretics, beta-blockers and lithium. Parenteral NSAIDs, particularly IN, DI and KE, have a clear role in the management of postoperative pain. Their efficacy is well proved in orthopedic surgery. Their use is contraindicated in patients with a history of

\*\*\*asthma\*\*\*, allergy, renal pathology or peptic ulceration.

SECTION HEADING: T Therapeutics  
 S Adverse Effects

CLASSIF. CODE: 35 Adverse Reactions  
 43 Analgesics, NSAIDs  
 44 Narcotics  
 66 Drug Interactions  
 69 Reviews

CONTROLLED TERM: PAIN \*TR; POSTOPERATIVE \*TR; IN-VIVO \*FT; CASES \*FT; INJECTION \*FT; ANTIINFLAMMATORY \*FT; REVIEW \*FT; RISK-FACTOR \*FT  
 [01] ANTIINFLAMMATORIES \*FT; MAIN-TOPIC \*FT; TR \*FT; AS \*FT; DI \*FT  
 [02] INDOMETACIN \*TR; INDOMETACIN \*AS; DICLOFENAC \*AS; DICLOFENAC \*TR; KETOROLAC \*TR; KETOROLAC \*AS; INDOMETACIN \*DI; DICLOFENAC \*DI; KETOROLAC \*DI; OXYCODONE \*TR; PETHIDINE \*TR; PENTANYL \*TR; MORPHINE \*TR; PAPAVERETUM \*TR; MORPHINE \*AS; ASPIRIN-LYSINE-SALT \*TR; KETOPROFEN \*TR; INDOPROFEN \*TR; TENOXICAM \*TR; PIROXICAM \*AS; OXYCODONE \*AS; PENTANYL \*AS; ASPIRIN \*AS; ALFENTANYL \*AS; MODE-OF-ACT. \*FT; ORTHOPEDICS \*FT; SURGERY \*FT; CONTRAINDICATION \*FT; DRUG-COMPARISON \*FT; I.V. \*FT; INJECTION \*FT; TR \*FT; AS \*FT; DI \*FT  
 FIELD AVAIL.: AB; LA; CT  
 FILE SEGMENT: Literature

L218 ANSWER 9 OF 19 DRUGU COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 1991-28479 DRUGU S Full-text  
 TITLE: A Prospective Study of Hospital Admissions Due to Drug Reactions.  
 AUTHOR: Leamont I; Dolphin R O; Baxter H; Morrison S; Hooke D H; McGrath S P  
 LOCATION: Melbourne, Australia  
 SOURCE: Aust. J. Hosp. Pharm. (21, No. 2, 90-95, 1991) 2 Fig. 4 Tab. 14  
 Ref.  
 CODEN: AUNPAI ISSN: 0310-6810  
 AVAIL. OF DOC.: Manager of Pharmaceutical Services, Monash Medical Center, Prince Henry's Hospital, St. Kilda Road, Melbourne, Vic. 3004, Australia.  
 LANGUAGE: English  
 DOCUMENT TYPE: Journal

## ABSTRACT:

67 Drugs were implicated in adverse drug reactions (ADRs) in 136/5423 hospital admissions (2.4%) in a 6-mth prospective study. Drugs included piroxicam, diclofenac, indometacin, diflunisal, ketoprofen, naproxen, cimetidine, doxycycline, warfarin, aspirin, dipyridamole, hydralazine, cyclopenthiadiazole, atenolol, metoprolol, digoxin, amiodarone, verapamil, nifedipine, chlorothiazide, methylglucamine, theophylline, allopurinol, ranitidine, methotrexate, glibenclamide, metformin, prochlorperazine, oxycodone, bromocriptine, thioridazine, naproxen, bleomycin, promethazine, morphine, allopurinol, co-trimoxazole, (trimethoprim + sulfamethoxazole), cyclophosphamide. Most ADRs were GI bleeding and cardiovascular complications;

5 were fatal.

SECTION HEADING: S Adverse Effects

CLASSIF. CODE: 18 Hematological  
 35 Adverse Reactions  
 43 Analgesics, NSAIDs  
 58 Vasoactive  
 66 Drug Interactions

CONTROLLED TERM: IN-VIVO \*FT; CASES \*FT; COMB. \*FT  
 [01] CYCLOPHOSPHAMIDE \*AS; CYCLOPHOSPHAMIDE \*DI; PANCYTOPENIA \*AS; MARROW-DISEASE \*AS; HEMOPTYSIS \*AS; HEMORRHAGE \*AS; CYSTITIS \*AS; BLADDER-DISEASE \*AS; WARFARIN \*DI; ASPIRIN \*DI; CYTOSTATICS \*FT; IMMUNOSUPPRESSIVES \*FT; CYCLOPHOS \*RN; AS \*FT; DI \*FT  
 CAS REGISTRY NO.: 50-18-0  
 [02] WARFARIN \*DI; WARFARIN \*AS; PANCYTOPENIA \*AS; MARROW-DISEASE \*AS; HEMOPTYSIS \*AS; HEMORRHAGE \*AS; CYSTITIS \*AS; HEMATEMESIS \*AS; MELENA \*AS; GASTROENTEROPATHY \*AS; HEMORRHAGE \*AS; EMBIS \*AS; GASTROENTEROPATHY \*AS; DEHYDRATION \*AS; ANEMIA \*AS; BLADDER-DISEASE \*AS; TRIMETHOPRIM \*DI; DOXYCYCLINE \*DI; SULFAMETHOXAZOLE \*DI; ASPIRIN \*DI; PREDNISOLONE \*DI; CIMETIDINE \*DI; CYCLOPHOSPHAMIDE \*DI; RODENTICIDES \*FT; ANTICOAGULANTS \*FT; WARFARIN \*RN; DI \*FT; AS \*FT  
 CAS REGISTRY NO.: 5543-58-8  
 [03] ASPIRIN \*DI; ASPIRIN \*AS; PANCYTOPENIA \*AS; MARROW-DISEASE \*AS; HEMOPTYSIS \*AS; HEMORRHAGE \*AS; CYSTITIS \*AS; HEMATEMESIS \*AS; MELENA \*AS; GASTROENTEROPATHY \*AS; HEMORRHAGE \*AS; ANEMIA \*AS; BLADDER-DISEASE \*AS; DICLOFENAC \*DI; DIFLUNISAL \*DI; DIPYRIDAMOLE \*DI; INDOMETACIN \*DI; KETOPROFEN \*DI; NAPROXEN \*DI; PIROXICAM \*DI; WARFARIN \*DI; PREDNISOLONE \*DI; CYCLOPHOSPHAMIDE \*DI; ANALGESICS \*FT; ANTIPYRETICS \*FT; ANTIRHEUMATICS \*FT; ANTIAGGREGANTS \*FT; PROSTAGLANDIN-ANTAGONISTS \*FT; ASPIRIN \*RN; DI \*FT; AS \*FT  
 CAS REGISTRY NO.: 50-78-2  
 [04] TRIMETHOPRIM \*DI; TRIMETHOPRIM \*AS; HEMATEMESIS \*AS; ANEMIA \*AS; CEREbroVASCULAR-DISEASE \*AS; MELENA \*AS; GASTROENTEROPATHY \*AS; HEMORRHAGE \*AS; EMBIS \*AS; GASTROENTEROPATHY \*AS; DEHYDRATION \*AS; MUCOSITIS \*AS; WARFARIN \*DI; CIMETIDINE \*DI; DOXYCYCLINE \*DI; ASPIRIN \*DI; PREDNISOLONE \*DI; CYCLOPHOSPHAMIDE \*DI; METHOTREXATE \*DI; COMB.PREP. \*FT; ANTISEPTICS \*FT; POLATE-ANTAGONISTS \*FT; TRIMETHOP \*RN; DI \*FT; AS \*FT  
 CAS REGISTRY NO.: 738-70-5  
 [05] SULFAMETHOXAZOLE \*AS; HEMATEMESIS \*AS; ANEMIA \*AS; CEREbroVASCULAR-DISEASE \*AS; MELENA \*AS; GASTROENTEROPATHY \*AS; HEMORRHAGE \*AS; EMBIS \*AS; GASTROENTEROPATHY \*AS; DEHYDRATION \*AS; MUCOSITIS \*AS; WARFARIN \*DI; CIMETIDINE \*DI; DOXYCYCLINE \*DI; ASPIRIN \*DI; PREDNISOLONE \*DI; CYCLOPHOSPHAMIDE \*DI; METHOTREXATE \*DI; COMB.PREP. \*FT; ANTISEPTICS \*FT; SULFAMETHOXAZOLE \*RN; AS \*FT  
 CAS REGISTRY NO.: 723-46-6  
 [06] DICLOFENAC \*AS; DICLOFENAC \*DI; HEMATEMESIS \*AS; MELENA \*AS; GASTROENTEROPATHY \*AS; HEMORRHAGE \*AS; ANEMIA \*AS; HEMOPTYSIS \*AS; HEMORRHAGE \*AS; ASPIRIN \*DI; ANTIINFLAMMATORIES \*FT; ANALGESICS \*FT; PROSTAGLANDIN-ANTAGONISTS \*FT; DICLOFENAC \*RN; AS \*FT; DI \*FT

CAS REGISTRY NO.: 15307-86-5  
[07] BLEOMYCIN \*AE; PULMONARY-FIBROSIS \*AE;  
PNEUMOPATHY \*AE; NEUTROPENIA \*AE; MARROW-DISEASE \*AE;  
THROMBOCYTOPENIA \*AE; ANTIBIOTICS \*PT; CYTOSTATICS \*PT;  
BLEOMYCIN \*RN; AE \*PT

CAS REGISTRY NO.: 11056-06-7  
[08] NAPROXEN \*AE; HEMATEMESIS \*AE; MELENA \*AE; GASTROENTEROPATHY  
\*AE; HEMORRHAGE \*AE; PROSTAGLANDIN-ANTAGONISTS \*PT;  
ANTIINFLAMMATORIES \*PT; ANALGESICS \*PT; ANTIPIRETTICS \*PT;  
NAPROXEN \*RN; AE \*PT

CAS REGISTRY NO.: 23204-53-1  
[09] DIGOXIN \*DI; DIGOXIN \*AE; BRADYCARDIA \*AE; ANOREXIA \*AE;  
HEART-BLOCK \*AE; ARRHYTHMIA \*AE; CARDIOPATHY \*AE; AMIODARONE  
\*DI; VERAPAMIL \*DI; ATENOLOL \*DI; NIFEDIPINE \*DI;  
CARDIOGLYCOSIDES \*PT; CARDIANTS \*PT; DIGOXIN \*RN; DI \*PT; AE  
\*PT

CAS REGISTRY NO.: 20830-75-5  
[10] CIMETIDINE \*AE; CIMETIDINE \*DI; HEMATEMESIS \*AE; ANEMIA \*AE;  
CEREBROVASCULAR-DISEASE \*AE; WARFARIN \*DI; TRIMETHOPRIM \*DI;  
SULFAMETHOXAZOLE \*DI; ANTIHISTAMINES-H2 \*PT; ANTIULCERS \*PT;  
GASTRIC-SECRETION-INHIBITORS \*PT; CIMETIDIN \*RN; AE \*PT; DI  
\*PT

CAS REGISTRY NO.: 151481-61-9  
[11] AMIODARONE \*DI; AMIODARONE \*AE; BRADYCARDIA \*AE; ARRHYTHMIA  
\*AE; CARDIOPATHY \*AE; ANOREXIA \*AE; DIGOXIN \*DI; VERAPAMIL  
\*DI; CALCIUM-ANTAGONISTS \*PT; CARDIANTS \*PT; ANTIARRHYTHMICS  
\*PT; AMIODARON \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 1951-25-3  
[12] VERAPAMIL \*DI; VERAPAMIL \*AE; ARRHYTHMIA \*AE; CARDIOPATHY  
\*AE; ANOREXIA \*AE; DIGOXIN \*DI; AMIODARONE \*DI; CARDIANTS  
\*PT; CALCIUM-ANTAGONISTS \*PT; VERAPAMIL \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 52-53-9  
[13] ATENOLOL \*DI; ATENOLOL \*AE; HEART-BLOCK \*AE; ARRHYTHMIA \*AE;  
CARDIOPATHY \*AE; DIGOXIN \*DI; NIFEDIPINE \*DI;  
SYMPATHOLYTICS-BETA \*PT; HYPOTENSIVES \*PT; ATENOLOL \*RN; DI  
\*PT; AE \*PT

CAS REGISTRY NO.: 29122-68-7  
[14] NIFEDIPINE \*DI; NIFEDIPINE \*AE; BRADYCARDIA \*AE; ARRHYTHMIA  
\*AE; CARDIOPATHY \*AE; DIGOXIN \*DI; ATENOLOL \*DI; CARDIANTS  
\*PT; CALCIUM-ANTAGONISTS \*PT; NIFEDIPIN \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 21829-25-4  
[15] METHYLDOPA \*DI; METHYLDOPA \*AE; ORTHOSTATIC \*AE; HYPOTENSION  
\*AE; VASCULAR-DISEASE \*AE; PERIPHERAL-NERVE-DISEASE \*AE;  
CHLOROTHIAZIDE \*DI; VERAPAMIL \*DI; CHLOROPROMAZINE \*DI;  
HYDRALAZINE \*DI; HYPOTENSIVES \*PT; SYMPATHOMIMETICS-ALPHA  
\*PT; METHYLDOP \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 555-30-6  
[16] CHLOROTHIAZIDE \*DI; CHLOROTHIAZIDE \*AE; ORTHOSTATIC \*AE;  
HYPOTENSION \*AE; VASCULAR-DISEASE \*AE; PERIPHERAL-NERVE-  
DISEASE \*AE; METHYLDOPA \*DI; VERAPAMIL \*DI; CHLOROPROMAZINE  
\*DI; CARBONIC-ANHYDRASE-INHIBITORS \*PT; DIURETICS \*PT;  
HYPOTENSIVES \*PT; CHLOROTH \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 58-94-6  
[17] CHLOROPROMAZINE \*DI; CHLOROPROMAZINE \*AE; ORTHOSTATIC \*AE;  
HYPOTENSION \*AE; VASCULAR-DISEASE \*AE; PERIPHERAL-NERVE-  
DISEASE \*AE; METHYLDOPA \*DI; CHLOROTHIAZIDE \*DI; VERAPAMIL  
\*DI; HYDRALAZINE \*DI; PSYCHOSEDATIVES \*PT; NEUROLEPTICS \*PT;  
SEDATIVES \*PT; DOPAMINE-ANTAGONISTS \*PT; CALMODULIN-  
ANTAGONISTS \*PT; CHLORPROM \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 50-53-3

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[18] HYDRALAZINE \*DI; HYDRALAZINE \*AE; ORTHOSTATIC \*AE;  
HYPOTENSION \*AE; VASCULAR-DISEASE \*AE; PERIPHERAL-NERVE-  
DISEASE \*AE; METHYLDOPA \*DI; VERAPAMIL \*DI; CHLOROPROMAZINE  
\*DI; METOPROLOL \*DI; CYCLOPENTHAZIDE \*DI; HYPOTENSIVES \*PT;  
HYDRALAZI \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 86-54-4  
[19] CYCLOPENTHAZIDE \*DI; CYCLOPENTHAZIDE \*AE; ORTHOSTATIC \*AE;  
HYPOTENSION \*AE; VASCULAR-DISEASE \*AE; PERIPHERAL-NERVE-  
DISEASE \*AE; METOPROLOL \*DI; HYDRALAZINE \*DI; DIURETICS \*PT;  
HYPOTENSIVES \*PT; CYPENTHA \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 742-20-1  
[20] DIFLUNISAL \*DI; DIFLUNISAL \*AE; HEMATEMESIS \*AE; MELENA \*AE;  
GASTROENTEROPATHY \*AE; HEMORRHAGE \*AE; ANEMIA \*AE; PIROXICAM  
\*DI; ANALGESICS \*PT; ANTIINFLAMMATORIES \*PT; ANTIPIRETTICS  
\*PT; PROSTAGLANDIN-ANTAGONISTS \*PT; DIFLUNISA \*RN; DI \*PT; AE  
\*PT

CAS REGISTRY NO.: 22494-42-4  
[21] PIROXICAM \*DI; PIROXICAM \*AE; HEMATEMESIS \*AE; MELENA \*AE;  
GASTROENTEROPATHY \*AE; HEMORRHAGE \*AE; ANEMIA \*AE; PIROXICAM  
\*DI; ANTIINFLAMMATORIES \*PT; PROSTAGLANDIN-ANTAGONISTS \*PT;  
PIROXICAM \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 36323-30-4  
[22] METOPROLOL \*DI; METOPROLOL \*AE; ORTHOSTATIC \*AE; HYPOTENSION  
\*AE; VASCULAR-DISEASE \*AE; PERIPHERAL-NERVE-DISEASE \*AE;  
CYCLOPENTHAZIDE \*DI; HYDRALAZINE \*DI; SYMPATHOLYTICS-BETA  
\*PT; METOPROLO \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 37350-58-6  
[23] DIPYRIDAMOLE \*DI; DIPYRIDAMOLE \*AE; MELENA \*AE;  
GASTROENTEROPATHY \*AE; HEMORRHAGE \*AE; ANEMIA \*AE; ASPIRIN  
\*DI; CARDIANTS \*PT; CALCIUM-ANTAGONISTS \*PT; ANTIAGGREGANTS  
\*PT; PHOSPHODIESTERASE-INHIBITORS \*PT; DIPYRIDAM \*RN; DI \*PT;  
AE \*PT

CAS REGISTRY NO.: 58-32-2  
[24] INDOMETACIN \*DI; INDOMETACIN \*AE; MELENA \*AE;  
GASTROENTEROPATHY \*AE; HEMORRHAGE \*AE; ASPIRIN \*DI;  
ANTIINFLAMMATORIES \*PT; ANTIPIRETTICS \*PT; ANTIRHEUMATICS  
\*PT; PROSTAGLANDIN-ANTAGONISTS \*PT; INDOMETAC \*RN; DI \*PT; AE  
\*PT

CAS REGISTRY NO.: 53-66-1  
[25] KETOPROFEN \*DI; KETOPROFEN \*AE; MELENA \*AE; GASTROENTEROPATHY  
\*AE; HEMORRHAGE \*AE; ANEMIA \*AE; ASPIRIN \*DI;  
ANTIINFLAMMATORIES \*PT; ANALGESICS \*PT; PROSTAGLANDIN-  
ANTAGONISTS \*PT; KETOPROFE \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 22071-15-4  
[26] DOXYCYCLINE \*DI; DOXYCYCLINE \*AE; HEMATEMESIS \*AE; MELENA  
\*AE; GASTROENTEROPATHY \*AE; HEMORRHAGE \*AE; EMESIS \*AE;  
GASTROENTEROPATHY \*AE; DEHYDRATION \*AE; WARFARIN \*DI;  
TRIMETHOPRIM \*DI; SULFAMETHOXAZOLE \*DI; ANTIMOTICS \*PT;  
DOXYCYCLI \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 564-25-0  
[27] PREDNISOLONE \*DI; PREDNISOLONE \*AE; HEMATEMESIS \*AE; MELENA  
\*AE; GASTROENTEROPATHY \*AE; HEMORRHAGE \*AE; ANEMIA \*AE;  
WARFARIN \*DI; ASPIRIN \*DI; CORTICOSTEROIDS \*PT; PDISOLON  
\*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 50-24-0  
[28] THEOPHYLLINE \*DI; THEOPHYLLINE \*AE; NAUSEA \*AE; EMESIS \*AE;  
GASTROENTEROPATHY \*AE; DEHYDRATION \*AE; ALLOPURINOL \*DI;  
RANITIDINE \*DI; BRONCHODILATORS \*PT; VASODILATORS \*PT;  
CARDIANTS \*PT; DIURETICS \*PT; ANTIASTHMATICS \*PT;  
PHOSPHODIESTERASE-INHIBITORS \*PT; THEOPHYLL \*RN; DI \*PT; AE

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[29] \*PT  
ALLOPURINOL \*DI; ALLOPURINOL \*AE; NAUSEA \*AE; EMESIS \*AE;  
GASTROENTEROPATHY \*AE; THEOPHYLLINE \*DI; ANTIGOUTS \*PT;  
ANTIINFLAMMATORIES \*PT; ALLOPURIN \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 315-30-0  
[30] RANITIDINE \*DI; RANITIDINE \*AE; ANOREXIA \*AE; NAUSEA \*AE;  
EMESIS \*AE; GASTROENTEROPATHY \*AE; THEOPHYLLINE \*DI;  
ANTIINFLAMMATORIES \*PT; ANTILULCERS \*PT; GASTRIC-SECRETION-  
INHIBITORS \*PT; RANITIDIN \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 66357-35-5  
[31] METHOTREXATE \*DI; METHOTREXATE \*AE; MUCOSITIS \*AE;  
TRIMETHOPRIM \*DI; SULFAMETHOXAZOLE \*DI; CYTOSTATICS \*PT;  
METHOTREX \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 59-05-2  
[32] GLIBENCLAMIDE \*DI; GLIBENCLAMIDE \*AE; HYPOGLYCEMIA \*AE;  
CARBOHYDRATE-METAB.DISORDER \*AE; CONFUSION \*AE;  
MENTAL-DISORDER \*AE; METFORMIN \*DI; ANTIHISTAMINES \*PT;  
GLIBENCLA \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 10238-21-8  
[33] METFORMIN \*DI; METFORMIN \*AE; HYPOGLYCEMIA \*AE;  
CARBOHYDRATE-METAB.DISORDER \*AE; CONFUSION \*AE;  
MENTAL-DISORDER \*AE; GLIBENCLAMIDE \*DI; ANTIHISTAMINES \*PT;  
METFORMIN \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 657-24-9  
[34] PROMETHAZINE \*DI; PROMETHAZINE \*AE; DYSTONIA \*AE; MYOPATHY  
\*AE; EXTRAPYRAMIDAL-DISORDER \*AE; ENCEPHALOPATHY \*AE;  
PROCHLORPERAZINE \*DI; ANTIHISTAMINES-H1 \*PT; SEDATIVES \*PT;  
PROMETHAZ \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 60-87-7  
[35] PROCHLORPERAZINE \*DI; PROCHLORPERAZINE \*AE; DYSTONIA \*AE;  
MYOPATHY \*AE; EXTRAPYRAMIDAL-DISORDER \*AE; ENCEPHALOPATHY  
\*AE; PROMETHAZINE \*DI; PSYCHOSEDATIVES \*PT; NEUROLEPTICS \*PT;  
ANTIEMETICS \*PT; DOPAMINE-ANTAGONISTS \*PT; PROCHLORP \*RN; DI  
\*PT; AE \*PT

CAS REGISTRY NO.: 58-38-5  
[36] MORPHINE \*DI; MORPHINE \*AE; CONFUSION  
\*AE; MENTAL-DISORDER \*AE; DROWSINESS \*AE; OXYCODONE  
\*DI; ANALGESICS \*PT; NARCOTICS \*PT; SEDATIVES \*PT;  
MORPHINE \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 57-27-2  
[37] OXYCODONE \*DI; OXYCODONE \*AE; CONFUSION  
\*AE; MENTAL-DISORDER \*AE; DROWSINESS \*AE; MORPHINE  
\*DI; ANALGESICS \*PT; NARCOTICS \*PT; SEDATIVES \*PT;  
OXYCODONE \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 74-42-6  
[38] BROMOCRIPTINE \*DI; BROMOCRIPTINE \*AE; CONFUSION \*AE;  
MENTAL-DISORDER \*AE; DROWSINESS \*AE; THIORIDAZINE \*DI;  
ANTIPARKINSONIANS \*PT; PROLACTIN-ANTAGONISTS \*PT;  
DOPAMINERGICS \*PT; BROMOCRIP \*RN; DI \*PT; AE \*PT

CAS REGISTRY NO.: 25614-03-3  
[39] THIORIDAZINE \*DI; THIORIDAZINE \*AE; CONFUSION \*AE;  
MENTAL-DISORDER \*AE; DROWSINESS \*AE; BROMOCRIPTINE \*DI;  
PSYCHOSEDATIVES \*PT; NEUROLEPTICS \*PT; DOPAMINE-ANTAGONISTS  
\*PT; CALMODULIN-ANTAGONISTS \*PT; THIORIDAZ \*RN; DI \*PT; AE  
\*PT

CAS REGISTRY NO.: 50-52-2  
FIELD AVAIL.: AB; LA; CT  
FILE SEGMENT: Literature

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ACCESSION NUMBER: 1988-10343 DRUGU T P S Full-text  
TITLE: Pain and Analgesics.  
AUTHOR: Kurz H von  
LOCATION: Munich, Germany, West  
SOURCE: Dtsch.Apoth.Ztg. (127, No. 52-53, 2747-57, 1987) 6 Fig. 10  
Tab. 20 Ref.

AVAIL. OF DOC.: CODEN: DAZE2 ISSN: 0011-9857  
Walthers-Straub-Institut fuer Pharmakologie und Toxikologie  
Nussbaumstrasse 26, 8000 Muenchen 2, West Germany.  
LANGUAGE: German  
DOCUMENT TYPE: Journal

## ABSTRACT:

The use of analgesics in the relief of pain is reviewed with reference to the  
opioids and NSAID, their indications, mechanism of activity, pharmacokinetics,  
dosage, side effects and interactions with other drugs. Agents that can elicit  
attacks of asthma, that interact with salicylates and that can be  
present in analgesic combinations without having analgesic properties are  
listed. The most serious danger of using opioids are respiratory paralysis  
after high doses of addiction following chronic use. NSAID have few side  
effects when taken sensibly, though they can occasionally induce asthma  
, Lyell's syndrome and possibly Reye's syndrome.

SECTION HEADING: T Therapeutics  
P Pharmacology  
S Adverse Effects

CLASSIF. CODE: 8 Pharmacokinetics  
35 Adverse Reactions  
43 Analgesics, NSAIDs  
44 Narcotics  
66 Drug Interactions  
69 Reviews

## CONTROLLED TERM:

[01] PAIN \*TR; ANALGESIC \*PT; REVIEW \*PT; CASES \*PT; IN-VIVO \*PT  
ANALGESICS \*PT; MAIN-TOPIC \*PT; TR \*PT; PH \*PT; DM \*PT; AE  
\*PT; DI \*PT

[02] PHENACETIN \*AE; PHENACETIN \*PH; PHENACETIN \*DI; PARACETAMOL  
\*TR; PARACETAMOL \*PH; PARACETAMOL \*DM; PARACETAMOL \*DI;  
PARACETAMOL \*AE; BUCETIN \*TR; BUCETIN \*DI; BUCETIN \*DM;  
BUCETIN \*AE; BUCETIN \*PH; PROPYPHENAZONE \*TR; PROPYPHENAZONE  
\*AE; ISOPYRIN \*PH; ISOPROPYLAMINOPHENAZONE \*PH;  
PROPYPHENAZONE \*DI; PROPYPHENAZONE \*DM; PROPYPHENAZONE \*PH;  
PHENAZONE \*TR; PHENAZONE \*AE; PHENAZONE \*DM; PHENAZONE \*DI;  
PHENAZONE \*PH; ISOPYRIN \*TR; ISOPROPYLAMINOPHENAZONE \*TR;  
ISOPYRIN \*AE; ISOPROPYLAMINOPHENAZONE \*AE; ISOPYRIN \*DM;  
ISOPROPYLAMINOPHENAZONE \*DM; ISOPYRIN \*DI;  
ISOPROPYLAMINOPHENAZONE \*DI; METAMIZOLE \*TR; METAMIZOLE \*PH;  
METAMIZOLE \*DI; METAMIZOLE \*DM; METAMIZOLE \*AE; IBUPROFEN  
\*TR; IBUPROFEN \*PH; IBUPROFEN \*DM; IBUPROFEN \*AE; IBUPROFEN  
\*DI; AZAPROPAZONE \*AE; DICLOFENAC \*AE; TR \*PT; AE \*PT; PH  
\*PT; DI \*PT; DM \*PT

[03] SALICYLATE \*DM; SALICYLATE \*AE; SALICYLATE \*DI; ASPIRIN \*TR;  
ASPIRIN \*AE; ASPIRIN \*PH; ASPIRIN \*DM; ASPIRIN \*DI;  
SALICYLAMIDE \*TR; SALICYLAMIDE \*PH; SALICYLAMIDE \*AE;  
SALICYLAMIDE \*DM; SALICYLAMIDE \*DI; ETHENZAMIDE \*TR;  
ETHENZAMIDE \*AE; ETHENZAMIDE \*PH; ETHENZAMIDE \*DI;

40

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

ETHENZAMIDE \*DM; SALACETAMIDE \*TR; SALACETAMIDE \*PH;  
SALACETAMIDE \*DI; SALACETAMIDE \*DM; SALACETAMIDE \*AR;  
BENORILATE \*TR; BENORILATE \*DM; BENORILATE \*AR; BENORILATE  
\*DI; BENORILATE \*PH; DIFLUNISAL \*TR; DIFLUNISAL \*PH;  
DIFLUNISAL \*AR; DIFLUNISAL \*DI; DIFLUNISAL \*DM; PHENACETIN  
\*TR; PHENACETIN \*DM; TR \*FT; AR \*FT; PH \*FT; DM \*FT; DI \*FT  
LEVOMETHADONE \*PH; NEFOPAM \*TR; NEFOPAM \*AR; NEFOPAM \*DI;  
NEFOPAM \*DM; NEFOPAM \*PH; OXYCODONE \*TR;  
OXYCODONE \*DI; OXYCODONE \*DM;  
OXYCODONE \*PH; OXYCODONE \*AR; PENTAZOCINE  
\*PH; PENTAZOCINE \*TR; PENTAZOCINE \*AR; PENTAZOCINE \*DI;  
PENTAZOCINE \*DM; PETHIDINE \*TR; PETHIDINE \*AR; PETHIDINE \*PH;  
PETHIDINE \*DI; PETHIDINE \*DM; PIRITRAMIDE \*TR; PIRITRAMIDE  
\*AR; PIRITRAMIDE \*DM; PIRITRAMIDE \*DI; PIRITRAMIDE \*PH;  
TILIDINE \*TR; TILIDINE \*AR; TILIDINE \*PH; TILIDINE \*DI;  
TILIDINE \*DM; TRAMADOL \*TR; TRAMADOL \*AR; TRAMADOL \*PH;  
TRAMADOL \*DI; TRAMADOL \*DM; SALICYLATE \*TR; DIACETYLMORPHINE  
\*TR; DIACETYLMORPHINE \*DM; DIACETYLMORPHINE \*PH;  
DIACETYLMORPHINE \*DI; DIACETYLMORPHINE \*DM; SALICYLATE \*PH;  
TR \*FT; PH \*FT; DI \*FT; AR \*FT; DM \*FT  
SUPRENORPHINE \*TR; CODEINE \*TR; DEXTROPROPOXYPHENE \*TR;  
SUPRENORPHINE \*DI; CODEINE \*DI; DEXTROPROPOXYPHENE \*DI;  
SUPRENORPHINE \*DM; CODEINE \*DM; DEXTROPROPOXYPHENE \*DM;  
SUPRENORPHINE \*PH; CODEINE \*PH; DEXTROPROPOXYPHENE \*PH;  
SUPRENORPHINE \*AR; CODEINE \*AR; DEXTROPROPOXYPHENE \*AR;  
DEXTROMORAMIDE \*TR; FENTANYL \*TR;  
HYDROMORPHONE \*TR; MORPHINE \*TR;  
DEXTROMORAMIDE \*PH; FENTANYL \*PH;  
HYDROMORPHONE \*AR; MORPHINE \*PH;  
DEXTROMORAMIDE \*DM; FENTANYL \*DM;  
HYDROMORPHONE \*DM; MORPHINE \*DM;  
DEXTROMORAMIDE \*DI; FENTANYL \*DI;  
HYDROMORPHONE \*DI; MORPHINE \*DI;  
DEXTROMORAMIDE \*AR; FENTANYL \*AR;  
HYDROMORPHONE \*PH; MORPHINE \*PH;  
LEVOMETHADONE \*TR; LEVOMETHADONE \*DM; LEVOMETHADONE \*AR;  
LEVOMETHADONE \*DI; TR \*FT; PH \*FT; AR \*FT; DM \*FT; DI \*FT  
FENOPROFEN \*AR; FLUFENAMATE \*AR; FLURBIPROFEN \*AR;  
INDOMETACIN \*AR; KETOPROFEN \*AR; NAPROXEN \*AR; NIFENAZONE  
\*AR; NIFLUMATE \*AR; OXYPHENBUTAZONE \*AR; PHENYLBUTAZONE \*AR;  
PIROXICAM \*AR; TOLMETIN \*AR; IRON-SALT \*DI; HEPARIN \*DI;  
CUMARIN \*DI; PROBENECID \*DI; SULFINPYRAZONE \*DI; ACLOFENAC  
\*AR; AMINOPHENAZONE \*AR; LACTYLPHENETIDINE \*TR;  
LACTYLPHENETIDINE \*AR; LACTYLPHENETIDINE \*PH;  
LACTYLPHENETIDINE \*DI; LACTYLPHENETIDINE \*DM; MTENAMATE \*AR;  
TR \*FT; AR \*FT; PH \*FT; DI \*FT; DM \*FT

FIELD AVAIL.:  
FILE SEGMENT:AB; LA; CT  
LiteratureL218 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2006 ACS ON STM  
ACCESSION NUMBER: 2006.1124928 CAPLUS Full-textDOCUMENT NUMBER: 145.443952  
TITLE:Compositions comprising aminergic compounds and  
complement compounds, such as ascorbates, cysteines,  
opioids, resveratrols, and polycarboxylic acid  
chelators  
Dillon, Patrick F.; Root-Bernstein, Robert S.

INVENTOR(S):

PATENT NO. KIND DATE APPLICATION NO. DATE  
WO 2006/113485 A2 20061026 WO 2006-US14165 20060414  
M: AR, AO, AL, AU, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,  
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GR,  
GH, GM, GN, GU, HR, HU, ID, IL, IN, JP, KE, KG, KM, KN, KP, KR,  
KZ, LC, LK, LR, LS, LT, LV, LY, MA, MD, MG, MK, MN, MW, MX,  
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RU, SC, SD, SE,  
SG, SK, SL, SM, SN, SY, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VC,  
VN, YU, ZA, ZM, ZW  
RM: AT, BR, BO, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,  
CF, CG, CI, CM, CA, GM, GN, GW, ML, MR, NE, SH, TD, TO, BM, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
KG, KZ, MD, RU, TJ, TM  
PRIORITY APPLN. INFO.: US 2005-672249 P 20050415  
US 2005-706249 P 20050805  
US 2005-738294 P 20051118

ED Entered STN: 27 Oct 2006  
AB Pharmaceutical compns. and method using aminergic compds. and complement  
compds. are provided comprising: (a) a subefficacious amount of a non-  
adrenergic aminergic compound or of an adrenergic antagonist; and (b) a safe  
and effective amount of a complement compound. Methods are also provided  
comprising the administration of: (a) a low dose of a non-adrenergic aminergic  
compound or any adrenergic antagonist; and (b) a safe and effective amount of  
a complement compound. Non-adrenergic aminergic compds. can comprise a  
histaminergic, dopaminergic, muscarinic, serotonergic, octopaminergic, or  
trace aminergic compound. Complement compds. include ascorbates, opioids,  
polycarboxylic acid chelators, resveratrols, cysteines, substituted deriva-  
tives, and analogs thereof, and mixtures thereof. Preferred complements include  
ascorbates, particularly ascorbic acid. Methods include the treatment of  
neural and neural disorders; mood and behavior disorders; cardiac, vascular,  
and cardiovascular disorders; hypertension, headache; respiratory disorders;  
gastrointestinal disorders; obesity; asthma, allergy; smooth muscle  
contraction disorders; nasal or nasopharyngeal conditions; genitourinary  
disorders; ocular disorders, glaucoma; and hormone- or neurotransmitter-  
release or -secretion disorders.

IT Bronchi, disease  
Inflammation  
(bronchitis; compns. comprising aminergic compound and  
complement compound for treatment of various disorders)

IT Lung, disease  
(chronic obstructive pulmonary disease;  
compns. comprising aminergic compound and complement compound for treatment  
of various disorders)

IT 5-HT agonists  
5-HT antagonists  
Allergy  
Alzheimer's disease  
Anticholinergics  
Asthma  
Bladder, disease

Blood vessel, disease  
Cardiovascular system, disease  
Chelating agents  
Combination chemotherapy  
Common cold  
Digestive tract, disease  
Dopamine agonists  
Dopamine antagonists  
Emphysema  
Epilepsy  
Eye, disease  
Glaucoma (disease)  
Headache  
Heart, disease  
Human  
Hypertension  
Influenza  
Mental and behavioral disorders  
Motion sickness  
Mouth, disease  
Movement disorders  
Muscarinic agonists  
Muscarinic antagonists  
Nervous system, disease  
Nose, disease  
Obesity  
Parkinson's disease  
Prostate gland, disease  
Respiratory system, disease  
Salivary gland, disease  
Schizophrenia  
Sexual disorders  
Sleep disorders  
Urticaria  
Vasodilation  
Adrenoceptor antagonists  
Adrenoceptor antagonists  
(compns. comprising aminergic compound and complement compound for  
treatment of various disorders)

IT Drug interactions  
(synergistic; compns. comprising aminergic compound and complement compound  
for treatment of various disorders)

IT 50-53-3, biological studies 50-55-5, Reserpine 50-60-2, Phentolamine  
50-67-9D, 5-Hydroxytryptamine, derivs. 50-81-7D, Ascorbic acid, analogs  
and derivs. 51-34-3, Scopalamine 51-45-6D, Histamine, derivs.  
51-55-8, Atropine, biological studies 51-61-6D, Haloperidol 52-90-4,  
L-Cysteine, biological studies 52-90-4D, L-Cysteine, N-(C1-18) acyl  
derivs. 54-80-8, Promethazine 55-65-2, Guanethidine 57-27-2,  
Morphine, biological studies 57-42-1, Meperidine 58-00-4, Apomorphine  
58-73-1, Diphenhydramine 59-96-1, Phenoxymethamine 59-98-3, Tolazoline  
60-00-4, EDTA, biological studies 63-75-2, Arecoline 69-23-8,  
Fluphenazine 70-22-4, Oxotremorine 76-41-5, Oxymorphone  
76-42-6, Oxycodone 76-57-3, Codeine 86-13-5,  
77-07-6, Levorphanol 82-58-6D, Lysergic acid, derivs. 86-13-5,  
Bentazapine 82-13-7, Pilocarpine 92-84-2D, Phenothiazine, derivs.  
93-65-2, 2-(12-Methyl-4-chlorophenoxy)propionic acid 107-35-7, Taurine  
107-15-7D, Taurine, N-(C1-18) acyl derivs. 110-89-4D, Piperidine,  
diphenylbutyl derivative 113-15-5, Ergotamine 125-28-0, Dihydrocodeine  
125-29-1, Hydrocodone 125-71-3, Dextromethorphan 129-03-3,

Cyproheptadine 134-03-2, Sodium ascorbate 146-48-5, Yohimbine  
155-58-8, Rhapontin 261-31-4D, Thioxanthene, derivs. 269-0-0,  
Amphetamine 359-83-1, Pentazocine 361-37-5, 364-62-5 437-38-7  
Pentamyl 458-24-2, Fenfluramine 465-65-6, Naloxone 465-99-9  
Hydrocortisone 469-62-5, Propoxyphene 483-04-5, Raubasine 483-10-3,  
Corynanthine 486-12-4, Triprolidine 490-83-5, Dehydroascorbic acid  
500-65-2, Rhapontigenin 501-36-0, Resveratrol 511-12-6,  
Dihydroergotamine 525-66-6, Propranolol 537-42-8, Pterostilbene  
561-27-3, Heroin 575-19-9 749-02-0, Epiperone 827-61-2, Aceclidine  
915-30-0, Diphenoxylate 1477-40-3, Levomefentanyl acetate 1977-10-2,  
Lorazepam 2706-56-1, 2-(2-Pyridyl)ethylamine 2709-56-0, Flupentixol  
2933-94-0, Toliprolol 3239-44-9, Dexfenfluramine 3576-73-6,  
2-Ethyl-8-methyl-2,8-diazaspiro[5.5]undecane-1,3-dione 3930-20-9, Sotalol  
5743-22-0, Mepranolol 5743-27-1, Calcium ascorbate 5786-21-0, Clozapine  
6452-71-7, Oxprenolol 6673-35-4, Praxetel 7413-36-7, Nifenalol  
7433-10-5, Butidrine 8006-25-5, Ergotamine 10083-24-6, Piceatannol  
11032-41-0, Dihydroergotamine 13523-86-9, Pindolol 13655-52-2,  
Alprenolol 14556-46-8, Bupranolol 15676-16-1, Sulpiride 17479-19-5,  
Dihydroergocristine 17692-51-2, Metergoline 18016-80-3, Lisuride  
19216-56-9, Prazosin 20229-30-5, Methiothepin 20594-83-6, Halbuphine  
21489-74-7, 2-Amino-5,6-dihydroxy-1,2,3,4-tetrahydronaphthalene  
22110-56-2, Ifenprodil 23594-81-7, Meptindolol 24219-97-4, Mianserin  
25447-65-0, Dihydroergocornine 25447-66-9, Dihydroergocryptine  
25523-97-1, Dexchlorpheniramine 25614-03-3, Bromocriptine 26839-75-8,  
Pimozide 26844-12-2, Indoramine 27848-84-6, Nicergoline 28797-61-7,  
Tirazepine 29122-68-7, Atenolol 29884-49-9, Astrinidin 30187-90-7,  
Xibenolol 34661-75-1, Urapidil 34915-68-9, Bunitrolol 34919-98-7,  
Cetamolol 35795-16-5, Trimazolin 36505-84-7, Buspirone 36894-69-6,  
Labetalol 37517-30-9, Acebutolol 38363-40-5, Penbutolol 39552-01-7,  
Befunolol 39563-28-5, Cloranolol 40580-59-4, Quandelol 42200-33-9,  
Nadolol 42408-82-2, Butorphanol 42438-89-1, Pinostilbene 47141-42-4,  
Levobunolol 50679-08-8, Terfenadine 51384-51-1, Metoprolol  
51481-61-9, Cimetidine 51781-06-7, Carteolol 52485-79-7, Buprenorphine  
53179-11-6, Loperamide 53648-55-8, Dezocine 53684-49-4, Bufetolol  
54063-51-3, Nadoxolol 54063-51-5, Propafenone 54340-58-8, Meptazinol  
54340-62-4, Bufuralol 54739-18-3, Fluvoxamine 54910-89-3, Fluoxetine  
55096-26-9, Nalmefene 55273-05-7, Iproridine 55837-25-7, Sufloxacin  
56030-54-7 56290-94-9, Medroxoalol 56980-93-9, Celiprolol  
57149-07-2, Naftopidil 57465-00-0, Talinolol 57536-86-4 57775-29-8,  
Carazolol 57808-66-9, Domperidone 58409-59-9, Bucumolol 58569-55-4,  
Met-enkephalin 58822-25-6, Leu-enkephalin 58930-32-8, Butofolol  
59170-23-9, Bevantolol 60607-68-3, Indenolol 61869-08-7, Paroxetine  
62658-63-3, Bopindolol 63590-64-7, Terazosin 63659-18-7, Betaxolol  
64795-35-3, Mesulergine 65119-89-3, Dimaprit 66104-22-1, Pergolide  
66264-77-5, Sulfinalol 66357-35-5, Ranitidine 66722-44-9, Bisooprolol  
67227-56-9, Fenoldopam 68377-92-4, Artanolol 69014-14-8, Tiotidine  
69906-85-0, Cyanopindolol 70904-56-7, Krotaphin 71119-11-4,  
Bucindolol 71195-58-9, Alfentanil 72822-12-9, Dapiprazole  
72956-09-3, Carvedilol 74050-98-9, Ketanserin 74135-04-9, Morpiceptin  
74191-85-8, Dexazosin 75659-07-3, Dilevalol 78950-78-4 79617-96-2,  
Sertraline 79944-58-4, Idazoxan 80373-22-4, Quinpirole 80755-51-7,  
Bunazosin 80880-90-6, Telentepine 81098-60-4, Cispripide 81147-92-4,  
Remolol 81403-80-7, Alfuzosin 81447-80-5, Diprafenone 81486-22-8,  
Nipradilol 81801-12-9, Xanotelol 82859-09-2, Combretastatin  
83166-66-9, Nefazodone 83688-84-0, Tertatolol 83928-76-1, Epiperone  
85006-82-2, Dynorphin B 85136-71-6, Tiliolol 85320-68-9, Aceazolol  
85550-52-8, Mirtazapine 86161-55-9, Onetol 86880-51-5, Spanolol  
87051-43-2, Ritanserin 88161-22-2, Dynorphin A 89565-68-4, Tropisetron  
98224-03-4, Eltopazine 98323-83-2, Carmoxirole 99614-02-5,  
Ondansetron 102203-18-9, Isetit 103628-46-2, Sumatriptan

106133-20-4, Tamsulosin 106243-16-7, Thiopramide 106266-06-2,  
Risperidone 107233-08-9, Cevimeline 109889-09-0, Granisetron  
112108-01-7, Scopolamine 115956-12-2, Dolasetron 118457-14-0, Nebivolol  
1121679-13-8, Naratriptan 125279-79-0, Erenitilide 131986-45-3,  
Xanomeline 132539-06-1, Olanzapine 133242-30-5, Landiolol  
139264-17-8, Zolmitriptan 139886-32-1, Milameline 142437-67-0,  
Amthamine 143322-58-1, Eletriptan 144034-80-0, Rizatriptan  
145231-45-4, Clobenpropit 147025-53-4, Talsclodine 151070-83-6,  
Isopropil 153601-03-7, Capsinolol 154323-57-6, Almotriptan 159912-53-5  
170912-52-4, Donitriptan

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(comps. comprising aminergic compound and complement compound for treatment of various disorders)

L218 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2006 ACS ON STN

ACCESSION NUMBER: 2006:322096 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 144:369762

TITLE: Preparation of biphenyl derivatives and analogs thereof as cannabinoid receptor ligands and methods of use

INVENTOR(S): Dolle, Roland E.; Worm, Karin; Zhou, O. Jean

PATENT ASSIGNER(S): Adolor Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 81 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

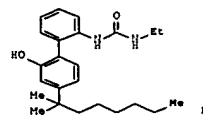
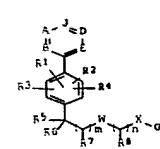
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| US 2006074086   | A1   | 20060406 | US 2005-242318  | 20051003 |
| WO 2006041841   | A1   | 20060420 | WO 2005-053567  | 20051004 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, ME, MG, MK, MN, MX, MY, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |          |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TO, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  |      |          |                 |          |
| PRIORITY APPL. INFO.: US 2004-616024P P 20041005  |      |          |                 |          |
| US 2005-242318 A 20051003   |      |          |                 |          |

OTHER SOURCE(S): MARPAT 144:369762

ED Entered STN: 07 Apr 2006

GI



AB Title compds. I (R1-4 independently = H, alkyl, alkoxy, etc.; R5 and R6 independently = H, alkyl or taken together with the carbon atom to which they are attached to form a 3-8-membered carbocyclic or heterocyclic ring; each R7 and R8 independently = H, alkyl, halo, etc.; J = N or (un)substituted C, provided that no more than two of A, B, D, E and J are N; A, B, D and E independently = N or (un)substituted C; G = alkyl, acyl, aryl, etc.; W = bond, O, S, CH2, etc.; X = bond, O, -CH2CH-, etc.; m and n independently = 1-5), and their pharmaceutical salts, are prepared and disclosed as cannabinoid receptor ligands. Thus, e.g., II was prepared by Suzuki coupling of 2-aminophenylboronic acid with resin bound bromophenol derivative (preparation described). Tested compds. were found to bind to human CB1 and/or CB2 receptor with affinity ranging from 0.1-5000 nM. Further, pharmaceutical compds. containing these compds., and methods for their pharmaceutical use are disclosed. In certain embodiments, the compds. are agonists and/or ligands of cannabinoid receptors and may be useful, inter alia, for treating and/or preventing pain, gastrointestinal disorders, genitourinary disorders, inflammation, glaucoma, auto-immune diseases, ischemic conditions, immune-related disorders, and neurodegenerative diseases, for providing cardioprotection against ischemic and reperfusion effects, for inducing apoptosis in malignant cells, and as an appetite stimulant.

IT Bronchi, disease  
Inflammation  
(bronchitis; preparation of biphenyl derivs. and analogs thereof as cannabinoid receptor ligands)

IT Lung, disease  
(chronic obstructive pulmonary disease; preparation of biphenyl derivs. and analogs thereof as cannabinoid receptor ligands)

IT Allergy  
Allergy inhibitors  
Alzheimer's disease  
Analgesics  
Anti-Alzheimer's agents  
Anti-ischemic agents  
Antiarhythmic  
Antiasthmatic  
Antidiabetic agents  
Antidiarrheals  
Antiemetics  
Antiglaucoma agents  
Antihypertensives  
Antiparkinsonian agents  
Antirheumatic agents  
Appetite stimulants  
Asthma  
Autoimmune disease

Bladder, disease  
Cachexia  
Celiac disease  
Combination chemotherapy  
Diabetes mellitus  
Diarrhea  
Digestive tract, disease  
Eating disorders  
Emphysema  
Gastrointestinal agents  
Glaucoma (disease)  
Human  
Hypertension  
Immune disease  
Immunomodulators  
Inflammation  
Ischemia  
Multiple sclerosis  
Myasthenia gravis  
Nausea  
Osteoporosis  
Pain  
Parkinson's disease  
Peoriasis  
Rheumatoid arthritis  
Sjogren syndrome  
Transplant and Transplantation  
Urogenital system, disease  
Vomiting  
(preparation of biphenyl derivs. and analogs thereof as cannabinoid receptor ligands)

IT 50-48-6 57-27-2, biological studies 57-41-0 57-42-1  
59-92-7, biological studies 76-41-5 76-42-6 76-57-3  
76-99-3 77-07-6 125-28-0 125-29-1 298-46-4, 5H-Dibenz[b,f]azepine-5-carboxamide 359-83-1 437-38-7 466-99-9 469-62-5  
768-94-5, Tricyclo[3.3.1.1.3.7]decan-1-amine 1972-08-3 2323-36-6  
13956-29-1 15686-91-6 20594-83-6 27203-92-5, Tramadol 28860-95-9,  
Carbidopa 42408-82-2 52485-79-7 53179-11-6 53648-55-8  
56030-54-7 60142-96-3 71195-50-9 84057-84-1  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(comps. for use in co-administration; preparation of biphenyl derivs. and analogs thereof as cannabinoid receptor ligands)

L218 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2006 ACS ON STN

ACCESSION NUMBER: 2005:1354741 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 144:94351

TITLE: A method of improving treatments in rheumatic and arthritic diseases using strontium salts

INVENTOR(S): Christgau, Stephan; Hansen, Christian; Nilsson, Henrik

PATENT ASSIGNER(S): Osteologix A/S, Den.

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXDS

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

|   |    |          |                |          |
|---|----|----------|----------------|----------|
| WO 2005123193   | A2 | 20051229 | WO 2005-DK404  | 20050617 |
| WO 2005123193   | A3 | 20060302 |                |          |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, ME, MG, MK, MN, MX, MY, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW     |    |          |                |          |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TO  |    |          |                |          |
| US 2004122174   |    | 20060608 | US 2005-269289 | 20051107 |
| WO 2006089546   | A1 | 20060831 | WO 2005-DK710  | 20051107 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, ME, MG, MK, MN, MX, MY, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |    |          |                |          |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TO, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  |    |          |                |          |

PRIORITY APPL. INFO.:

|                |    |          |
|----------------|----|----------|
| DK 2004-950    | A  | 20040617 |
| DK 2003-691    | A  | 20030507 |
| DK 2003-932    | A  | 20030620 |
| DK 2003-1870   | A  | 20031209 |
| US 2003-52442P | P  | 20031209 |
| WO 2004-DK328  | A2 | 20040506 |
| WO 2005-DK140  | A2 | 20050228 |
| WO 2005-DK401  | A2 | 20050617 |
| WO 2005-DK404  | A2 | 20050617 |

ED Entered STN: 30 Dec 2005

AB Improved treatments of joint diseases, such as, e.g. osteoarthritis and rheumatoid arthritis, and pain, comprise a strontium-containing compound administered alone or in combination with one or more second therapeutically and/or prophylactically active substances. The second active substance is selected from the group consisting of bisphosphonates, glucosamine, palliative agents, analgesic agents, disease modifying anti-rheumatic compds. (DMARDs), selective estrogen receptor modulators (SERMs), aromatase inhibitors, non-steroidal anti-inflammatory agents (NSAIDs), COX-2 inhibitors, COX-3 inhibitors, opioids, inhibitors/antagonists of IL-1, inhibitors/antagonists of TNF- $\alpha$ , inhibitors of matrix metallo-proteinases (MMPs), cathepsin K inhibitors, inhibitors/antagonists of RANK-ligand, statins, glucocorticoids, chondroitin sulfate, HMG-A receptor antagonists, inhibitors of interleukin-1 converting enzyme, Calcitonin gene related peptide antagonists, glycine antagonists, vanilloid receptor antagonists, inhibitors of inducible nitric oxide synthetase (iNOS), N-acetylcholine receptor agonists, neurokinin antagonists, neuroleptic agents, PAR2 receptor antagonists and anabolic growth factors acting on joint tissue components. Pharmaceutical compns. comprising a strontium-containing compound and a second therapeutically and/or prophylactically active substance as defined above are also described. Thus, a tablet formulation to be administered one to two times daily contained elendronate 10 mg, strontium malonate 200 mg, lactose

Piroxicam 38194-50-2, Sulindac 40182-75-20, Stenstrom citrate 40391-99-9  
40472-00-2 41340-25-4, Stodolac 41593-31-1,  
Dihydrochrysenes 41839-80-9 42408-08-2, Butorphanol 42924-53-8,  
Nabumetone 51146-56-6, Dexibuprofen 515-37-3, Budesonide 51800-78-2, Minoxidil 5248-81-7, Bupropion 5359-27-6, Fendosal 53965-13-3, Cyclosporine 60118-07-2, Endorphin 63524-05-0  
66376-36-1, Alendronate 67763-96-6, Inaulin-like growth factor-1  
68047-06-3, 4-Hydroxytamoxifen 71125-38-7, Meloxicam 74103-06-3,  
Ketorolac 77599-17-8, Panomifene 78994-23-7, Levomecloxiline 81093-37-0, Pravestatin 82413-20-5, Droloxifen 84449-90-1, Raloxifene 85801-42-9  
86111-26-4, Zindoxifene 89000-95-2, Oligon-like peptide 2 89778-26-7, Toremfine 89958-99-9, Tilduridine 9395-9-1, Fluvastatin 95730-99-9, ICI 102454-24-6  
98774-23-3, Temilifene 103735-76-8, erythro-MDA 105462-24-6 114084-78-5, Ibandronate 115674-74-3, TAT-59 116057-75-1  
105462-24-6 118072-93-8, Zoledronate 121268-58-9, Olpadronate 123663-49-0, T-614 128607-22-7 129453-61-8  
129612-87-9, Mipiroxifen 130996-28-0, P 54 134195-17-8, Cyclodextrin sulfate 134523-00-5, Atorvastatin 135459-87-9, Strontium ranelate 137945-48-3, CT 3 138330-18-4, Incadronate 143090-92-0, Anakinra 145599-86-6, Cerivastatin 158048-95-2, 8-2474 15816-4-1, 103323 161799-44-4, Ketorolac sulfate 170713-75-4, Noreceptin 175031-36-0, NCX 179649-40-00 strontium diformate 180064-38-4 180916-16-9,  
Lasofoxiene 182167-03-9, EM-800 189954-66-3, DFP 190791-29-8, CO-336156 192755-52-5, Pralnacasin 194841-32-2, Bazedoxifene 278172-05-7  
307370-87-2 322766-10-9, Tiracoxib 507471-54-7 507471-56-7  
615258-40-7, AAM 162 610395-06-1, SVT 2016 796104-84-2 796104-86-4  
796104-90-0 796644-36-9 796842-37-0 796842-38-1 796842-39-1  
872049-77-8 872049-79-0 872049-81-2 872049-83-2 872049-85-9 872049-87-8  
872049-89-0 872049-91-7 872049-92-8 872049-93-9 872049-94-0 872049-95-1 872049-95-9 872125-28-5  
RL: THU (Therapeutic use): BIOL (Biological study): USKS (Uses)  
(oral combination of strontium salt and other agents for improvement in treatment of arthritic diseases and associated pain)

L218 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2005:1354712 CAPLUS Full-text  
DOCUMENT NUMBER: 144:94350  
TITLE: A method of improving the medical treatment of pain  
AUTHOR(S): Christgau, Stephan; Hansen, Christian; Nilsson, Henrik  
PATENT ASSIGNEE(S): Osteologix A/S, Den.  
SOURCE: PCT Int. Appl., 34 pp.  
CODEN: P1XXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 9  
PATENT INFORMATION:

| PATENT NO.  | KIND   | DATE      | APPLICATION NO. | DATE      |
|-------------|--|-----------|-----------------|-----------|
| 20050123192 | A2   | 200501229 | 200505-DK401    | 200506167 |
| W:          | AR, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GR, GU, HK, HU, IL, IN, JP, KS, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ZY |           |                 |           |
| RW:         | BW, GR, GM, GE, LS, MW, MJ, NA, SD, SL, SZ, TZ, UG, ZW, ZM, AZ, BY, BG, KE, MD, RU, TJ, TM, AT, BS, BG, CH, CY, CZ, DE, DK,  |           |                 |           |

76-57-3, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 77-17-8, Norbuprenorphine 79-17-4, Aminoguanidine 84-02-6, Compazine 103-90-2, Paracetamol 113-59-7, Taraxacin 117-89-5, Trifluoperazine 125-29-1, Hydrocodone 130-61-0, Mellaril 151-16-6, S-(2-Aminoethyl)isothiourea 359-83-1, Pentazocine 364-62-5, Metoclopramide 437-38-7, Fentanyl 440-17-5, Stelazine 466-93-9, Hydromorphone 548-73-2, Inapsine 561-27-3, Heroin 526-26-1, Strontium ascorbate 548-73-2, 1977-10-2, Loxapine 2034-23-3, PR 038251 868-19-9, Strontium citrate 1977-10-2, 1986-19-8, S-Methyl-L-arginine 20594-83-6, Oxazepam 2149-70-8, 1986-19-8, S-Methylisothiourea 2986-20-1, S-Ethylisothiourea 4456-77-3, PR 038470 4673-26-1 5104-49-9, Flurbiprofen 5588-33-0, Gerezitil 5591-45-7, Navane 5786-21-0, Clozaril 6913-17-3, S-Isopropylisothiourea 7232-21-5, Reglan 7166-34-4, Molindone 13539-59-8, Apazone 15307-86-5, Diclofenac 15622-65-8, Moban 15687-27-1, Ibuprofen 16067-69-9, Strontium benzenesulfonate 16088-89-4 17035-93-4, N-Monomethyl-L-arginine 20594-83-6, Naproxen 2149-70-8, 1986-19-8, Ketofol 22204-53-1, Naproxen 2149-70-8, 1986-19-8, Ibuprofen 16067-69-9, Strontium citrate 1977-10-2, 1986-19-8, Tramadol 27833-61-3, Loxitane 29679-58-1, Fenoprofen 32672-69-5, Mesoridazine besylate 36322-90-4, Piroxicam 37841-91-1, Isovellral 38194-50-2, Sulindac 40182-75-0, Strontium citrate 40472-00-2 41839-80-9 42408-82-2, Butorphanol 51803-78-2, Nimesulide 52485-79-7, Buprenorphine 53648-55-8, Dezocine 53774-63-3 58493-49-5, Olvanil 61595-50-8, Scutigerol 61595-50-8, Meloxicam 78754-81-1, PR 19133 83002-04-1, 1982-06-6, 10626-06-2, Risperdal 111974-69-7, Clozapine 111974-72-2, Serquel 123663-49-0, T-614 128007-31-8, Arvanil 123539-06-1, Zyprexa 133587-00-5, N-Monomethyl-L-arginine acetate 135459-87-9, Strontium ranelate 146939-27-7, Geodon 158362-52-5, BW373UB6 156719-41-4, S-Methyl-L-thiocitrulline 158089-95-3, S-2474 159860-31-8, SNC-121 175031-36-0, NCK401 179469-40-0 181313-72-4, Strontium malonate 182293-82-5 189954-66-3, PR 19470-05-7, Parecoxib 198470-85-6, Dynastat 251362-87-5 27842-02-5, 1982-06-6, 10626-06-2, 122766-90-0, Tirofiban 34942-92-3, SB-366791 507471-56-9 535974-91-4 630395-06-1, SVT 2016 796104-16-6 796104-86-4 796104-90-0 796842-36-9 796842-37-0 796842-38-1 872049-77-9 872049-78-0 872049-79-1 872049-81-5 872049-83-7 872049-85-0 872049-86-0 872049-88-2 872049-89-3 872049-90-6 872049-91-7 872049-92-8 872049-93-9 872049-94-6 872049-95-1 872125-28-8 872200-43-6 872340-68-6, AZD 4717

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(method of improving medical treatment of pain by administering combination of strontium-containing compound and second active substance)

1218 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2006 ACS ON STN  
ACCESSION NUMBER: 2005:1078238 CAPLUS Full-text  
DOCUMENT NUMBER: 143:373327  
TITLE: Pharmaceutical active substance  
combination comprising substituted carbinol  
compounds and non-steroidal anti-inflammatory drugs  
INVENTOR(S): Buechmann, Helmut Heinrich; Gutierrez, Silva  
Bonifacio; Holenz, Jorg; Farre, Gonis Antonio  
PATENT ASSIGNER(S): Spain  
SOURCE: U.S. Pat. Appl. Publ., 26 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
PATENT ACC. NUM. COUNT: 2  
PARENT INFORMATION:

49

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2005222136 | A1   | 20051006 | US 2004-987803  | 20041112 |
| CA 2562219    | AA   | 20051020 | CA 2005-2562219 | 20050405 |
| WO 2005097099 | A1   | 20051020 | WO 2005-EP3641  | 20050405 |

W: AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GO, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: ES 2004-4000844 A 20040405  
ES 2004-844 A 20040405  
US 2004-987803 A 20041112  
WO 2005-EP3641 W 20050405

OTHER SOURCE(S): MARPAT 143:373327

ED Entered STM: 07 Oct 2005

AB The present invention relates to an active substance combination including at least one substituted carbinol compound and at least one non-steroidal anti-inflammatory drug (NSAID), a medicament including the active substance combination, a pharmaceutical formulation including the active substance combination and the use of the active substance combination for the manufacture of a medicament.

TI Pharmaceutical active substance combination comprising substituted carbinol compounds and non-steroidal anti-inflammatory drugs

ST pharmaceutical combination substituted carbinol compd nonsteroidal antiinflammatory drug

IT Urogenital system  
(-related pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Inflammation  
(Crohn's disease; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Intestine, disease  
(Crohn's; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal  
(Hodkin's disease; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal  
(Peutz-Jegher syndrome; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal  
(Scleroderma; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drugs of abuse  
(abuse of, treatment and prevention of; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

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IT Pain  
(acute; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Carcinoma  
(adenocarcinoma; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Swelling, biological  
(after injury; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Transplant and Transplantation  
(allotransplant, cornea, rejection; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Heart, disease  
(angina pectoris, pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Blood vessel, neoplasm  
(angiofibroma, nasopharynx; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Inflammation  
Spinal column, disease  
(ankylosing spondylitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Anemia (disease)  
(aplastic; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal  
(arthropathy, Bursitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal  
(back pain, lower, chronic pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Body, anatomical  
(back, disease, pain, lower, chronic pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Pain  
(back, lower, chronic pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Skin, neoplasm  
(basal cell carcinoma; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Carcinoma  
(basal cell; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Injury  
(bone, pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

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non-steroidal anti-inflammatory drugs)

IT Bronchi, disease  
Inflammation  
(bronchitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Epithelium  
(cancer effecting; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Lip  
(cancer; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(capsules; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Ischemia  
(cardiac; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Pain  
(central, post-operative; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Uterus, neoplasm  
(cervix, carcinoma; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Carcinoma  
(cervix; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Pain  
(chronic; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Headache  
(cluster; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Intestine, neoplasm  
(colon; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Eye, disease  
Inflammation  
(conjunctivitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Eye  
(cornea, allotransplant, rejection; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Transplant rejection  
(corneal; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Bladder, disease

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Inflammation  
(cystitis, pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Pain  
(dental; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Mental and behavioral disorders  
(depression; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Eye, disease  
(diabetic retinopathy; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Joint, anatomical  
(disease, Bursitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Viscera  
(disease, pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Joint, anatomical  
(disease, sprain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Tendon  
(disease, tendinitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(dragees; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(drops; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Uterus, disease  
(endometriosis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(enteric-coated; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Alcohols, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(fatty; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Ulcer  
(gastric; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Inflammation  
Stomach, disease  
(gastritis; pharmaceutical active substance

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combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(gels; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Gingiva, disease  
Inflammation  
(gingivitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(granules; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Bladder, disease  
(incontinence; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal  
(infantile hemangiomas; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Intestine, disease  
(inflammatory; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(injections, i.m.; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(injections, i.p.; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(injections, i.v.; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(injections, s.c.; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Bone, disease  
(injury, pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Autoimmune disease  
(insulin-dependent diabetes mellitus; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Diabetes mellitus  
(insulin-dependent; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(intrathecal; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Intestine, disease

(irritable bowel syndrome; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Heart, disease  
(ischemia; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Rheumatoid arthritis  
(juvenile; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(liq.; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Angiogenesis  
(mediated disorder; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Neoplasm  
(metastasis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Hydrocarbon waxes, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(microcryst.; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Headache  
(migraine; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(mucosal, transmucosal; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(nasal; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Pharynx  
(nasopharynx, angiofibroma; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Glaucoma (disease)  
(neovascular; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Angiogenesis  
(neovascularization, eye; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Eye, disease  
(neovascularization; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Kidney, disease  
(nephrotic syndrome; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Nerve, disease  
Pain  
(neuralgia, Herpes; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Inflammation  
(neurogenic; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Nerve, disease  
(neuropathy, pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Nerve  
(nociceptive, pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Anti-inflammatory agents  
(non-steroidal; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(oral; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Burn  
Head and Neck  
Perforation  
Sunburn  
Surgery  
Tooth, disease  
(pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(parenteral; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(pellete; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Artery, disease  
Inflammation  
(periarthritis nodosa; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Arm  
Leg  
(phantom limb pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Analgesics  
Anti-infective agents  
Anti-inflammatory agents  
Antiarthritics  
Antiepileptics  
Antidepressants  
Antidiabetic agents  
Antirheumatic agents

Antitumor agents  
Antiulcer agents  
Antiviral agents  
Arthritis  
Asthma  
Beeswax  
Behcet's syndrome  
Bladder, neoplasm  
Blood vessel, disease  
Bone, neoplasm  
Brain, neoplasm  
Carcinoma  
Common cold  
Dermatitis  
Digestive tract, disease  
Digestive tract, neoplasm  
Dysmenorrhea  
Eczema  
Edema  
Fever and Hyperthermia  
Gelation agents  
Gout  
Headache  
Inflammation  
Influenza  
Liver, neoplasm  
Lung, neoplasm  
Mammary gland, neoplasm  
Myasthenia gravis  
Myositis  
Neoplasm  
Opioid antagonists  
Osteoarthritis  
Ovary, neoplasm  
Pancreas, neoplasm  
Plasticizers  
Prostate gland, neoplasm  
Psoriasis  
Rheumatic fever  
Rheumatoid arthritis  
Sarcoidosis  
Skin, disease  
Skin, neoplasm  
Strain  
(pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Carneuba wax  
Fats and Glyceric oils, biological studies  
Fatty acids, biological studies  
Opioids  
Polymers, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Myositis  
(polymyositis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(rectal; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Kidney, neoplasm  
(renal cell carcinoma; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Carcinoma  
(renal cell; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Eye  
(retina, neovascularisation; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Eye, disease  
(retrolental fibroplasia; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(orals; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Spinal column, disease  
(spondyloarthropathy; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal  
(sprain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Carcinoma  
(squamous cell; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(suspensions; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(sustained-release; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Injury  
(swelling; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Arthritis  
Synovial membrane, disease  
(synovitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Waxes  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(synthetic; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(syrups; pharmaceutical active substance combination

comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Lupus erythematosus  
(systemic; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(tablets, immediate release; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(tablets; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Inflammation  
(tendinitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Inflammation  
Thyroid gland, disease  
(thyroiditis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems  
(transdermal; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Stomach, disease  
(ulcer; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Inflammation  
Intestine, disease  
(ulcerative colitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Bone, disease  
(vascular necrosis of bone; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Infection  
(viral; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal  
(visceral pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Pain  
(visceral; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT 561-27-3, Diacetylmorphine  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(heroin; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT 50-33-9, Phenylbutazone, biological studies 50-78-2, Acetylsalicylic acid 53-86-1, Indomethacin 56-81-5, 1,2,3-Propanetriol, biological studies 57-27-2, Morphine, biological studies 57-42-1,

Pethidine 61-68-7, Mefenamic acid 62-67-9, Nalorphine 65-45-2, Salicylamide 67-56-1, Carbinol, biological studies 68-89-3, Metamizol 71-50-1, Acetate, biological studies 76-41-5, Oxymorphone 76-42-6, Oxycodone 76-57-3, Codeine 76-58-4, Ethylmorphine 77-07-6, Levorphanol 92-43-3, Phenidone 103-90-2, Paracetamol 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 125-58-6, Levomethadone 129-20-3, Oxypentazone 152-02-3, Levallorphan 288-13-1, Pyrazole 288-32-4, Imidazole, biological studies 302-41-0, Piritramide 357-56-2, Dextromoramide 359-83-1, Pentazocine 437-38-7, Fentanyl 465-65-6, Mefenone 466-99-5, Hydromorphone 469-62-3, Dextropropoxyphene 469-79-4, Ketobenzidone 479-92-5, Propoxyphene 530-78-9, Flufenamic acid 644-62-2, Meclofenamic acid 853-34-9, Kebuzone 915-10-0, Diphenoxylate 938-73-8, Ethenzamide 1477-40-3, Levomethadyl 2210-63-1, Mefebutazone 2438-72-4, Bufenamac 4394-00-7, Niflumic acid 5104-49-4, Flurbiprofen 9004-34-6D, Cellulose, ester 9004-57-3, Ethyl cellulose 14521-96-3, Strophine 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16590-41-3, Maltrexone 20594-03-6, Nalbuphine 21256-18-8, Oxapropzin 21363-18-8, Viminal 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22494-42-4, Diflunisal 24171-32-3, Tolmetin 27201-92-5, Tramadol 29679-58-1, Fenoprofen 30231-64-8, Glycerol monobenhenate 30544-47-9, Etofenamate 30748-29-9, Feprazone 31566-31-1, Glycerol monostearate 33005-95-7, Tiaprofenic acid 34552-84-6, Isoxicam 36322-90-4, Piroxicam 36330-85-5, Fenbufen 38194-50-2, Sulindac 41340-25-4, Etodolac 42408-82-2, Butorphanol 42924-53-8, Nabumetone 51803-78-2, Nimesulide 51931-66-9, Tilidine 52485-79-7, Buprenorphine 53164-05-9, Acemetacin 53179-11-6, Loperamide 53648-55-8, Desocine 53808-88-1, Lonazolac 54340-58-8, Meptazinol 56030-54-7, Bupentanil 59804-37-4, Tenoxicam 66532-85-2, Propacetamol 70374-39-9, Lornoxicam 71125-38-7, Meloxicam 71195-59-9, Alfentanil 74103-06-3, Ketorolac 112344-52-2, Plobuten 122154-30-7 122154-31-8 122154-32-9 122154-33-0 122154-35-2 122154-36-3 122154-37-4 122154-38-5 122154-39-6 122154-40-9 122154-41-0 122154-42-1 122154-43-2 122154-44-3 122154-45-4 122154-46-5 122154-47-6 122154-49-8 122154-51-2 122154-52-3 122154-53-4 122154-55-6 122154-56-7 122154-57-8 122154-60-3 122154-63-6 122154-67-0 122154-68-1 122154-69-2 122154-70-5 122154-71-6 122154-72-7 122154-73-8 122154-74-9 122154-75-0 122154-76-1 122154-77-2 122154-78-3 122154-79-4 122154-80-7 122154-81-8 122154-82-9 122154-83-0 122154-84-1 122154-85-2 122154-86-3 122154-87-4 122154-88-5 122154-89-6 122154-90-9 122154-91-0 122154-92-1 122154-93-2 122154-94-3 122154-95-4 122154-96-5 122154-97-6 122154-98-7 122154-99-8 122155-00-4 122155-01-5 122155-02-6 122155-03-7 122155-04-8 122155-06-0 122155-08-2 122155-09-3 122155-10-4 122155-11-5 122155-12-6 122155-13-7 122155-14-4 122155-15-5 122155-16-6 122155-17-7 122155-18-1 122155-19-6 122155-20-8 122155-21-9 122155-22-0 122155-23-1 122155-24-2 122155-25-3 122155-26-4 122155-27-5 122155-28-6 122155-29-7 122155-30-0 122155-31-1 122155-32-2 122155-33-3 122155-34-4 122155-35-5 122155-36-6 122155-37-7 122155-38-8 122155-39-9 122155-40-2 122155-41-3 122155-42-4 122155-43-5 122155-44-6 122155-45-7 122155-46-8 122155-47-9 122155-48-0 122155-49-1 122155-50-4 122155-51-5 122155-52-6 122155-53-7 122155-54-8 122155-55-9 122155-56-0 122155-57-1 122155-58-2 122155-59-3 122155-60-4 122155-61-5 122155-62-6 122155-63-7 122155-64-0 122155-65-1 122155-66-2 122155-67-3 122155-68-4 122155-69-5 122155-70-8 122155-71-9 122155-72-0 122155-73-1 122155-74-2 122155-75-3 122155-76-4 122155-77-5 122155-78-6 122155-79-7 122155-80-0 122155-81-1 122155-82-2 122155-83-3 122155-84-4 122155-85-5 122155-86-6 122155-87-7 122155-88-8 122155-89-9 122155-90-2 122155-91-3 122155-92-4 122155-93-5 122155-94-6 122175-88-6 122175-89-7 122175-90-0 122175-91-1 122175-92-2

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT 122175-93-3 122175-94-4 122175-95-5 122175-96-6 122175-97-7 122175-98-8 122175-99-9 122176-00-5 122176-01-6 131575-03-6 14-Methoxymetopon 132875-61-7, Remifentanyl 142155-43-9 145981-63-9 148981-65-1 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 181695-72-7, Valdecoxib 198470-84-7, Parecoxib 202409-33-4, Etoricoxib 247046-52-2 247046-53-3 247046-54-4 247046-55-5 247046-56-6 247046-57-7 247046-58-8 247046-59-9 247046-60-2 247046-61-3 247046-62-4 247046-63-5 247046-64-6 247046-65-7 247046-66-8 247046-67-9 247046-68-0 247046-69-1 247046-70-4 247046-71-5 247046-72-6 251375-82-3 258329-57-6 258329-58-8 258329-61-2 258329-62-3 258329-63-4 258329-64-5 258329-65-6 258329-66-7 258329-67-8 258329-68-9 258329-69-0 258329-70-3 258329-71-4 258329-72-5 258329-73-6 258329-74-7 258329-76-9 258329-77-0 258329-78-1 866218-44-2 866218-45-3 866218-46-4 866218-47-5 866218-48-6 866218-49-7

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

L218 ANSWER 16 OF 19 WPX COPYRIGHT 2006 THE THOMSON CORP ON STN  
ACCESSION NUMBER: 2005-296105 [30] WPX  
DOC. NO. CPI: C2005-091570 [30]  
TITLE: Use of a spirocyclic heterocyclic compound for binding an opioid receptor in the treatment of e.g. pain, gastrointestinal dysfunction  
DERIVAT CLASS: B02; B03  
INVENTOR: AJELLO C W; CHU G; DOLLE R E; GU M; LE BOURDONNEC B; LEISTER L K; TUTHILL P A; ZHOU J Q; ZHOU Q J; AJELLO C; DOLLE R; LEISTER L; TUTHILL P; ZHOU J  
PATENT ASSIGNER: (ADOL-N) ADOLOR CORP; (AJEL-1) AJELLO C W; (CHU-1) CHU G; (DOLL-1) DOLLE R E; (GU-1) GU M; (LBDOU-1) LE BOURDONNEC B; (LEIS-1) LEISTER L K; (TUTH-1) TUTHILL P A; (ZHOU-1) ZHOU Q J  
COUNTRY COUNT: 107

PATENT INFO ABBR.:  
PATENT NO KIND DATE WEEK LA PG MAIN IPC  
WO 2005033073 A2 20050414 (200530) EN 573[0]  
US 20050159438 A1 20050721 (200540) EN  
EP 1675847 A2 20060705 (200644) EN

APPLICATION DETAILS:  
PATENT NO KIND APPLICATION DATE  
WO 2005033073 A2 WO 2004-0532479 20041001  
US 20050159438 A1 Provisional US 2004-0756449 20031001  
US 20050159438 A1 US 2004-957554 20041001  
EP 1675847 A2 EP 2004-817130 20041001  
EP 1675847 A2 EP 2004-0524729 20041001



## FILING DETAILS:

| PATENT NO  | KIND | PATENT NO                |
|------------|------|--------------------------|
| EP 1675847 | A2   | Based on WO 2005033073 A |

PRIORITY APPLN. INFO: US 2003-507864P 20031001  
US 2004-957554 20041001

## TECH

**ORGANIC CHEMISTRY** - Preferred Compounds: (I') comprise compounds of formula (I'a):

R1 and R3 = H, alkyl, alkenyl, alkynyl or aryl;  
Z = -N(R5)-;  
R2 = H, (cyclo)alkyl, alkenyl, alkynyl, alkylcycloalkyl or (hetero)aryl;  
R1-R3, R1-R2 and R2-R3 = 4-8-membered heterocycloalkyl ring;  
Ra = H or alkyl;  
Rb = H, alkyl or aryl;  
n = 0-3;  
A and B' = H, fluoro or alkyl;  
A-B' = a double bond between the carbon atoms to which they are attached;  
R4 = -Y-W;  
Y = a single bond, C(Ra)(Rb), C(Ra)(Rb)(C(Ra)(Rb) or C(Ra)(Rb)(C(Ra)(Rb)(C(Ra)(Rb));  
W = (hetero)aryl;  
X = -CH2-, -O-, -S-, -SO2 or -N(R5)-;  
R5 = H, (cyclo)alkyl, -(CH2)-alkenyl, -(CH2)-alkynyl, aryl, -CORb or -SO2Rb;  
J-carbon atoms to which it is attached = 6-membered aryl or 5- or 6-membered heteroaryl ring.  
Provided that:  
(a) when R2 is other than -CH(C(=O)-ORb)(Ra), then R1-R2 and R2-R3 form 4-8-membered heterocycloalkyl ring; when J taken together with the carbon atoms to which it is attached forms phenyl optionally mono- to tri-substituted by -S-1-4C alkyl, 1-4C alkyl (both optionally substituted by at least one halo or 1-4C alkoxy); halo or ORb, W is unsubstituted naphthyl or phenyl optionally mono- to tri-substituted by halo, 1-6C alkyl, 1-6C alkoxy, phenyl, phenoxy, 1,3-benzodioxazolyl, 2,2-difluoro-1,3-benzodioxazolyl, HW2, -N(1-4C alkyl)2 or pyrrollyl; n is 1; R1 and R3 are H; A-B forms a double bond between atoms to which they are attached; Y is a single bond; and X is -O-; then R2 is other than H or methyl; when J taken together with the carbon atoms to which it is attached forms a phenyl ring; W is phenyl optionally mono- to tri-substituted by fluoro, ORb, 1-6C alkoxy (optionally substituted by at least one fluoro), 2-6 alkenyl or -S-1-4C alkyl; n is 1; R1 and R3 are H; A-B' forms a double bond between atoms to which they are attached; Y is a single bond; and X is -O-; then R2 is other than H or benzyl; and when J forms a 6-membered aryl ring, then it is substituted with other than pyrimidine-2,4-diamine-meth-5-yl.  
In (I'), the spiro carbon and/or the carbon to which -Y-W is attached (preferably the carbon to which -Y-W is attached, or the spiro carbon and the carbon to which -Y-W is attached) is chiral. Preparation: (i) can be prepared by 37 methods as given in the specification e.g. preparation of (ia) (where X is CH or H) involves:  
(a) condensing 2'-hydroxyacetophenone derivative of formula (i) with 1-Boc-4-piperidone in pyrrolidone derivative of formula (ii) at room temperature to obtain N-Boc-spiro(2H-1-benzopyran-2,4'-piperidine)-4(3H)-one derivative of formula (iii);  
(b) converting (iii) into an enol triflate derivative of formula (v) using

N-phenylbis(trifluoromethanesulfonamide) of formula (iv) as a triflating agent; and  
(c) coupling (v) by Suzuki type coupling with 4-(N,N-diethylaminocarbonyl)phenyl boronic acid (vi) in ethylene glycol dimethyl ether in the presence of tetrakis triphenylphosphine palladium(0) (10 wt. % on activated carbon), lithium chloride and aqueous solution of sodium carbonate to obtain a substituted spiro(2H-1-benzopyran-2,4'-piperidine) compound of formula (viii), followed by conversion under acidic conditions. Ru-Ry = not defined.  
**PHARMACEUTICALS** - Preferred Composition: The composition further comprises an antibiotic, antiviral, antifungal, anti-inflammatory and/or anesthetic. Preferred Drugs: The opioid is selected from 73 drugs(s), or their diastereomers, salts or complexes as given in the specification e.g. allylprodine, dextromoramide, etazocine, fentanyl, ketobesidone, loperamide, lofentanil, morphine, piritramide, tilidine. The agent for the treatment of neuropathic pain is a mild OTC analgesic, a narcotic analgesic, an antiseizure medication or an anti-depressant. The agent for the treatment of depression is a selective serotonin re-uptake inhibitor, a tricyclic compound, a monoamine oxidase inhibitor or an antidepressant compound belonging to the heterocyclic class. The agent for the treatment of incontinence is an anticholinergic agent, an antispasmodic medication, a tricyclic antidepressant, a calcium channel blocker or a beta agonist. An agent for the treatment of Parkinson's disease is selected from deprenyl, amantadine, levodopa or carbidopa. Preferred Method: The prevention or treatment of pain with (I) further involves administering an opioid. The prevention or treatment of urogenital tract disorder with (I) further involves administering an agent for the treatment of incontinence. The prevention or treatment of depression with (I) further involves administering an agent for the treatment of depression. The prevention or treatment of tremors with (I) further involves administering an antiparkinsonian agent. The production or maintenance of an anesthetic state with (I) further involves administering an anesthetic agent selected from an inhaled anesthetic, a hypnotic, an anxiolytic, a neuromuscular blocker or an opioid.

L218 ANSWER 17 OF 19 WPX COPYRIGHT 2006 THE THOMSON CORP ON STN  
ACCESSION NUMBER: 2006-030913 [04] WPX  
DOC. NO. CPI: C2006-011203 [04]  
TITLE: Use of opioid controlled release oral dosage form for treating chronic obstructive pulmonary disease  
DERIVAT CLASS: B02  
INVENTOR: FLEISCHER W; LEYENDECKER P; REIMER K  
PATENT ASSIGNEE: (EURO-H) EUROCELTIQUE SA  
COUNTRY COUNT: 110  
PATENT INFO ABBR.:  
PATENT NO KIND DATE WEEK LA PG MAIN IPC  
EP 1604666 A1 20051214 (200604) EN 24 [0]  
WO 2005120507 A1 20051222 (200604) EN

## APPLICATION DETAILS:

| PATENT NO        | KIND | APPLICATION    | DATE     |
|------------------|------|----------------|----------|
| EP 1604666 A1    |      | WP 2004-13468  | 20040608 |
| WO 2005120507 A1 |      | WP 2005-EPE155 | 20050608 |

PRIORITY APPLN. INFO: EP 2004-13468 20040608  
TECH

**PHARMACEUTICALS** - Preferred Dosage: The dosage comprises an opioid agonist (e.g. oxycodone, hydrocodone, hydromorphone, morphine, methadone, oxycodone, fentanyl or sufentanyl in the form of free base or salt) or a mixture of opioid agonist and opioid antagonist (e.g. naltrexone, naloxone or naloxone in the form of free base or salt). Preferably the dosage comprises oxycodone, morphine or a mixture of oxycodone (10 - 150, preferably 10 - 80 mg) and naloxone (1 - 50 mg). Oxycodone and naloxone are present in a ratio up to 25:1 (preferably up to 20:1, especially 2:1 or 1:1). Preferably amount of oxycodone is higher than that of naloxone. The compounds are released from the dosage in a sustained, invariant or independent manner.

## CONTROLLED TERM:

Medical Descriptors:  
\*short course therapy  
\*cancer pain: CO, complication  
\*cancer pain: DT, drug therapy  
\*chronic pain: CO, complication  
\*chronic pain: DT, drug therapy  
\*neuropathic pain: CO, complication  
\*neuropathic pain: DT, drug therapy  
\*proactive study  
\*medical audit  
\*analgesic activity  
\*receptor blocking  
\*drug safety  
\*drug efficacy  
\*world health organization  
\*lung cancer  
\*head and neck cancer  
\*breast cancer  
\*skin cancer  
\*prostate cancer  
\*kidney cancer  
\*colorectal cancer  
\*fragility fracture  
\*drowsiness: SI, side effect  
\*confusion: SI, side effect  
\*hallucination: SI, side effect  
\*human  
\*male  
\*female  
\*clinical article  
\*controlled study  
\*aged  
\*adult  
\*article  
\*priority journal  
\*Drug Descriptors:  
\*ketamine: AE, adverse drug reaction  
\*ketamine: CB, drug combination  
\*ketamine: DT, drug therapy  
\*ketamine: IV, intravenous drug administration  
\*narcotic analgesic agent: AE, adverse drug reaction  
\*narcotic analgesic agent: CB, drug combination  
\*narcotic analgesic agent: DT, drug therapy  
\*narcotic analgesic agent: IV, intravenous drug administration  
\*antiinflammatory agent: AE, adverse drug reaction  
\*antiinflammatory agent: CB, drug combination  
\*antiinflammatory agent: DT, drug therapy  
\*antiinflammatory agent: IV, intravenous drug administration  
\*nonsteroid antiinflammatory agent: AE, adverse drug reaction  
\*nonsteroid antiinflammatory agent: CB, drug combination  
\*nonsteroid antiinflammatory agent: DT, drug therapy  
\*nonsteroid antiinflammatory agent: IV, intravenous drug administration  
\*steroid: AE, adverse drug reaction  
\*steroid: CB, drug combination  
\*steroid: DT, drug therapy

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ACCESSION NUMBER: 2005081426 EMBASE Full-text  
TITLE: Prospective audit of short-term concurrent ketamine, opioid and anti-inflammatory ('triple-agent') therapy for episodes of acute on chronic pain.  
AUTHOR: Good P.; Tullio P.; Jackson K.; Goodchild C.; Ashby M.  
CORPORATE SOURCE: Prof. M. Ashby, Centre for Palliative Care, St. Vincent's Hospital, University of Melbourne, PO Box 2900, Fitzroy, Vic. 3065, Australia. ashby@netspace.net.au  
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SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 3 Mar 2005  
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**ABSTRACT:** Aim: This prospective audit was undertaken in order to document the analgesic response and adverse effects of concurrent short-term ('burst') triple-agent analgesic (ketamine, an opioid and an anti-inflammatory agent - either steroidal or non-steroidal) administration, for episodes of acute on chronic pain. The clinical hypothesis in this study is that better pain control may be obtained by simultaneous multiple target receptor blockade. Method: The response of 18 patients is reported. The pain and analgesic requirement data for the 24 h before starting triple-agent therapy were compared with the last 24 h on the triple-agent therapy. Patients were then classified as responders or non-responders. Results: According to stringent clinical criteria, 12 out of the 18 patients were classified as responders. The response rate was highest for somatic pain (7/9) and appeared to decrease with duration of prior uncontrolled pain. Only four out of the 18 patients reported adverse effects and all of these were minor. Conclusions: The results suggest that this 'burst' triple-agent approach is safe and effective in an inpatient palliative care population during episodes of poorly controlled acute on chronic pain, and warrants further investigation to ascertain whether it gives superior results compared to the 'gold-standard' WHO ladder approach.

steroid: IV, intravenous drug administration  
ketorolac: AE, adverse drug reaction  
ketorolac: CB, drug combination  
ketorolac: DT, drug therapy  
ketorolac: IV, intravenous drug administration  
naproxen: AE, adverse drug reaction  
naproxen: CB, drug combination  
naproxen: DT, drug therapy  
naproxen: IV, intravenous drug administration  
dexamethasone: AE, adverse drug reaction  
dexamethasone: CB, drug combination  
dexamethasone: DT, drug therapy  
dexamethasone: IV, intravenous drug administration  
parecoxib: AE, adverse drug reaction  
parecoxib: CB, drug combination  
parecoxib: DT, drug therapy  
parecoxib: IV, intravenous drug administration  
morphine: AE, adverse drug reaction  
morphine: CB, drug combination  
morphine: DO, drug dose  
morphine: DT, drug therapy  
morphine: IV, intravenous drug administration  
hydromorphone: AE, adverse drug reaction  
hydromorphone: CB, drug combination  
hydromorphone: DO, drug dose  
hydromorphone: DT, drug therapy  
hydromorphone: IV, intravenous drug administration  
oxycodone: AE, adverse drug reaction  
oxycodone: CB, drug combination  
oxycodone: DO, drug dose  
oxycodone: DT, drug therapy  
oxycodone: IV, intravenous drug administration  
prednisolone: AE, adverse drug reaction  
prednisolone: CB, drug combination  
prednisolone: DO, drug dose  
prednisolone: DT, drug therapy  
(ketamine) 1867-66-9, 6740-88-1, 81771-21-3; (ketorolac)  
74101-06-3; (naproxen) 22204-53-1, 26159-34-2;  
(dexamethasone) 50-02-2; (parecoxib) 198470-84-7,  
198470-85-8; (morphine) 52-26-6, 57-27-2; (hydromorphone)  
466-99-9, 71-68-1; (oxycodone) 124-90-3, 76-42-6;  
(prednisolone) 50-24-8

## CAS REGISTRY NO.:

L218 ANSWER 19 OF 19 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN  
ACCESSION NUMBER: 200016057 EMBASE Full-text  
TITLE: Managing addiction in advanced cancer patients: Why Bother?  
AUTHOR: Passik S.D.; Theobald D.S.  
CORPORATE SOURCE: Dr. S.D. Passik, Community Cancer Care Inc., 115 West 19th Street, Indianapolis, IN 46202, United States  
SOURCE: Journal of Pain and Symptom Management, (2000) Vol. 19, No. 3, pp. 229-234.  
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FILE SEGMENT: 032 Psychiatry

036 Health Policy, Economics and Management  
037 Drug Literature Index  
040 Drug Dependence, Alcohol Abuse and Alcoholism  
008 Neurology and Neurosurgery

LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 13 Apr 2000  
Last Updated on STN: 13 Apr 2000

ABSTRACT: The management of addiction in patients with advanced cancer can be time-consuming, labor-intensive, and difficult. Some clinicians believe that it is not worth the effort, due in part to a failure to appreciate the deleterious impact of addiction on palliative care efforts and a view of addiction as intractable in any case. Indeed, it is possible that some clinicians perceive addiction not only fatalistically but, because of common misconceptions, believe that managing or attempting to decrease the patient's use of alcohol or illicit substances would be tantamount to depriving a dying patient of a source of pleasure. In this paper, we argue that managing addiction is an essential aspect of palliative care for chemically-dependent and alcoholic patients. The goal of such efforts is not complete abstinence, but exerting enough control over illicit drug and alcohol use to allow palliative care interventions to decrease suffering. To illustrate this view, we describe two patients with chemical dependency. We highlight the impact of unchecked substance abuse on patient's perpetuation of their own suffering, the complication of symptom management, the diagnosis and treatment of mood/anxiety disorders, and the effect on the patients' family and caregivers. Copyright (c) 2000 U.S. Cancer Pain Relief Committee.

CONTROLLED TERM: Medical Descriptors:  
\*addiction  
\*cancer patient  
palliative therapy  
drug abuse  
anxiety neurosis: ET, etiology  
anxiety neurosis: DT, drug therapy  
anxiety neurosis: CO, complication  
smoking  
advanced cancer  
alcoholism: TH, therapy  
group therapy  
adenocarcinoma  
pleura metastasis: SU, surgery  
pleura effusion: TH, therapy  
drain  
withdrawal syndrome: PC, prevention  
withdrawal syndrome: DT, drug therapy  
cancer pain: DT, drug therapy  
cancer pain: CO, complication  
patient information  
caregiver  
insomnia: DT, drug therapy  
insomnia: CO, complication  
heroin dependence  
lung cancer: RT, radiotherapy  
human  
male  
case report  
adult  
article  
Drug Descriptors:  
alcohol

illicit drug  
lorazepam: DT, drug therapy  
lorazepam: CB, drug combination  
oxycodone: DT, drug therapy  
oxycodone: CB, drug combination  
paracetamol: DT, drug therapy  
paracetamol: CB, drug combination  
trazodone: DT, drug therapy  
trazodone: CB, drug combination  
fentanyl: DT, drug therapy  
fentanyl: CB, drug combination  
fentanyl: TD, transdermal drug administration  
fentanyl: IV, intravenous drug administration  
(alcohol) 64-17-5; (lorazepam) 846-49-1; (oxycodone)  
124-90-3, 76-42-6; (paracetamol) 103-90-2; (trazodone)  
19794-93-5, 25332-39-2; (fentanyl) 437-38-7

FILE 'HOME' ENTERED AT 11:13:55 ON 14 DEC 2006

## SEARCH HISTORY

→ d his nofile

(FILE 'HOME' ENTERED AT 09:53:23 ON 14 DEC 2006)

FILE 'CAPLUS' ENTERED AT 09:53:50 ON 14 DEC 2006

D SAVED  
ACT ARN458CAAUL/A  
-----  
L1 1 SEA ABB-ON US2003-661458/APPS  
-----  
L2 141 SEA ABB-ON PACE G7/AU  
L3 11003 SEA ABB-ON SMITH M7/AU  
L4 1 SEA ABB-ON L2 AND L3  
D SCAN

FILE 'STINGUIDE' ENTERED AT 09:54:39 ON 14 DEC 2006

FILE 'REGISTRY' ENTERED AT 09:55:54 ON 14 DEC 2006

L5 1 SEA ABB-ON MORPHINE/CN  
L6 1 SEA ABB-ON FENTANYL/CN  
L7 1 SEA ABB-ON SUFFENTANIL/CN  
L8 1 SEA ABB-ON ALFENTANYL/CN  
L9 1 SEA ABB-ON OXYMORPHONE/CN  
L10 1 SEA ABB-ON HYDROMORPHONE/CN  
L11 1 SEA ABB-ON OXYCODONE/CN

FILE 'CAPLUS' ENTERED AT 09:56:07 ON 14 DEC 2006

L12 31087 SEA ABB-ON (L5 OR L6 OR L7 OR L8 OR L9 OR L10)  
L13 1073 SEA ABB-ON L11  
D SCAN L4  
L14 12914 SEA ABB-ON OPIOIDS/CT  
L15 1209 SEA ABB-ON L14(L)KAPPA/OBI  
L16 1944 SEA ABB-ON L14(L)MU/OBI  
L17 56591 SEA ABB-ON AGONIST8/OBI  
L18 368 SEA ABB-ON L15(L)L17  
L19 454 SEA ABB-ON L16(L)L17  
L20 19117 SEA ABB-ON RESPIRATORY TRACT/OBI  
L21 76 SEA ABB-ON L20(L)CARCINOMA/OBI  
L22 25232 SEA ABB-ON ASTHMA/OBI  
L23 424 SEA ABB-ON BRONCHIECTASIS/OBI OR BRONCHI?/OBI(L)DILATATION/OBI  
OR KARTAGENER/OBI  
L24 28786 SEA ABB-ON TUBERCULOSIS/OBI  
L25 4089 SEA ABB-ON BRONCHITIS/OBI  
L26 120 SEA ABB-ON RESPIRATORY SYSTEM, NEOPLASM/CT  
L27 35560 SEA ABB-ON LUNG, NEOPLASM/CT  
L28 4992 SEA ABB-ON CHRONIC OBSTRUCTIVE PULMONARY/OBI OR COPD/OBI  
L29 7726 SEA ABB-ON BRONCHOPNEUMONIA/OBI OR PNEUMONIA/OBI  
L30 136 SEA ABB-ON LARYNGITIS/OBI  
L31 1101 SEA ABB-ON SINUSITIS/OBI  
L32 2601 SEA ABB-ON EMPHYSEMA/OBI  
L33 6378 SEA ABB-ON FIBROSING/OBI(L)ALVEOLITIS/OBI OR (PULMONARY/OBI  
OR LUNG/OBI OR RESPIRATORY/OBI) (L) (FIBROSIS/OBI OR SARCOIDOSIS/  
OBI)  
L34 6 SEA ABB-ON SLEEP DISORDERS/CT(L)RESPIRATORY/OBI  
L35 943 SEA ABB-ON SLEEP/OBI(L)APNEA/OBI  
L36 1691 SEA ABB-ON SARCOIDOSIS/CT  
L37 39125 SEA ABB-ON DRUG INTERACTIONS-OLD,MT/CT  
L38 4450 SEA ABB-ON DRUG DELIVERY SYSTEMS-OLD/CT(L)CONG?/OBI

L39 16989 SEA ABB-ON COMBINATION CHEMOTHERAPY/CT  
L40 5480 SEA ABB-ON COMB7/OBI(L)PHARMAC7/OBI  
L41 6 SEA ABB-ON (L12 OR L19) AND (L13 OR L18) AND (L21 OR L22 OR  
L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR  
L32 OR L33 OR L34 OR L35 OR L36) AND (L37 OR L38 OR L39 OR  
L40)  
L42 552 SEA ABB-ON (L12 OR L19) (L) (COMB7/OBI OR COADMIN7/OBI OR  
CODRUG7/OBI OR CONCOMITANT7/OBI OR CONCURRENT7/OBI OR BLEND7/OB  
I OR MIXTURE7/OBI)  
L43 82 SEA ABB-ON (L13 OR L18) (L) (COMB7/OBI OR COADMIN7/OBI OR  
CODRUG7/OBI OR CONCOMITANT7/OBI OR CONCURRENT7/OBI OR BLEND7/OB  
I OR MIXTURE7/OBI)  
L44 3 SEA ABB-ON L42 AND L43 AND (L21 OR L22 OR L23 OR L24 OR L25  
OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33 OR L34  
OR L35 OR L36)  
L45 5 SEA ABB-ON ((L42 AND L43) OR (L12 OR L19) AND (L13 OR L18)  
AND (L37 OR L38 OR L39 OR L40))) AND (L2 OR L3)  
  
FILE 'EMBASE' ENTERED AT 10:09:18 ON 14 DEC 2006  
L46 83 SEA ABB-ON PACE G7/AU  
L47 8120 SEA ABB-ON SMITH M7/AU  
L48 53452 SEA ABB-ON MORPHINE/CT  
E FENTANYL/CT  
E B3-ALL  
L49 26736 SEA ABB-ON FENTANYL/CT OR FENTANYL CITRATE/CT  
E SUFENTANIL/CT  
L50 4395 SEA ABB-ON SUFENTANIL/CT OR SUFENTANIL CITRATE/CT  
E ALFENTANIL/CT  
E B5-ALL  
L51 4482 SEA ABB-ON ALFENTANIL/CT  
E OXYMORPHONE/CT  
L52 805 SEA ABB-ON OXYMORPHONE/CT  
E HYDROMORPHONE/CT  
L53 2957 SEA ABB-ON HYDROMORPHONE/CT  
E OXYCODONE/CT  
L54 3754 SEA ABB-ON OXYCODONE/CT  
E ASTHMA-ALL/CT  
L55 84233 SEA ABB-ON ASTHMA-NT/CT  
E BRONCHIECTASIS-ALL/CT  
L56 4535 SEA ABB-ON BRONCHIECTASIS-NT/CT  
E PULMONARY TUBER/CT  
E B4-ALL  
E B2-ALL  
L57 15140 SEA ABB-ON LUNG TUBERCULOSIS/CT  
E COPD/CT  
E B3-ALL  
E B2-ALL  
L58 26377 SEA ABB-ON CHRONIC OBSTRUCTIVE LUNG DISEASE/CT  
E BRONCHITIS-ALL/CT  
L59 22047 SEA ABB-ON BRONCHITIS-NT/CT  
E BRONCHOPNEUMONIA-ALL/CT  
L60 2275 SEA ABB-ON BRONCHOPNEUMONIA/CT  
E LARYNGITIS-ALL/CT  
L61 2500 SEA ABB-ON LARYNGITIS-NT/CT  
E SINUSITIS-ALL/CT  
L62 12991 SEA ABB-ON SINUSITIS-NT/CT  
E EMPHYSEMA-ALL/CT  
L63 13249 SEA ABB-ON EMPHYSEMA-NT/CT  
E FIBROSING ALV/CT  
E B4-ALL

73

L64 2738 SEA ABB-ON FIBROSING ALVEOLITIS/CT  
E PULMONARY FIBROSIS/CT  
E B3-ALL  
E B2-ALL  
L65 19527 SEA ABB-ON LUNG FIBROSIS-NT/CT  
E SARCOID/CT  
E SARCOIDOSIS/CT  
E B3-ALL  
L66 11397 SEA ABB-ON SARCOIDOSIS/CT  
E LUNG CANCER/CT  
L67 91685 SEA ABB-ON LUNG CANCER-NT/CT  
E SLEEP APNEA-ALL/CT  
E B3-ALL  
L68 11977 SEA ABB-ON SLEEP APNEA SYNDROME/CT  
L69 20 SEA ABB-ON (L46 AND L47) OR ((L46 OR L47) AND (L48 OR L49 OR  
L50 OR L51 OR L52 OR L53) AND L54)  
L70 0 SEA ABB-ON (L46 AND L47)  
L71 10397 SEA ABB-ON (L47 OR L48 OR L49 OR L50 OR L51 OR L52 OR  
L53) (L) (CB OR IT)/CT  
L72 493 SEA ABB-ON L54(L) (CB OR IT)/CT  
L73 5 SEA ABB-ON L71 AND L72 AND (L46 OR L47)  
L74 5 SEA ABB-ON (L46 AND L47) OR (L71 AND L72 AND (L46 OR L47))  
D TRIAL 1-5  
L75 38068 SEA ABB-ON DRUG POTENTIATION/CT  
L76 1228 SEA ABB-ON MU OPIATE RECEPTOR AGONIST/CT  
L77 949 SEA ABB-ON KAPPA OPIATE RECEPTOR AGONIST/CT  
L78 208 SEA ABB-ON L76(L) (CB OR IT)/CT  
L79 149 SEA ABB-ON L77(L) (CB OR IT)/CT  
L80 10397 SEA ABB-ON (L48 OR L49 OR L50 OR L51 OR L52 OR L53) (L) (CB OR  
IT)/CT  
L81 5 SEA ABB-ON (L46 AND L47) OR (L80 AND L72 AND (L46 OR L47))  
L82 0 SEA ABB-ON (L48 OR L49 OR L50 OR L51 OR L52 OR L53 OR L76)  
AND (L77 OR L54) AND L75 AND (L55 OR L56 OR L57 OR L58 OR L59  
OR L60 OR L61 OR L62 OR L63 OR L64 OR L65 OR L66 OR L67 OR  
L68)  
L83 820 SEA ABB-ON (L72 OR L79) OR (L80 OR L78) AND (L55 OR L56 OR  
L57 OR L58 OR L59 OR L60 OR L61 OR L62 OR L63 OR L64 OR L65 OR  
L66 OR L67 OR L68)  
L84 2 SEA ABB-ON (L72 OR L79) AND (L80 OR L78) AND (L55 OR L56 OR  
L57 OR L58 OR L59 OR L60 OR L61 OR L62 OR L63 OR L64 OR L65 OR  
L66 OR L67 OR L68)  
D TRIAL 1-2

FILE 'DRUGU' ENTERED AT 10:26:08 ON 14 DEC 2006

L85 2 SEA ABB-ON PACE G7/AU  
L86 1100 SEA ABB-ON SMITH M7/AU  
D TRIAL L85 1-2  
L87 9457 SEA ABB-ON (L5 OR L6 OR L7 OR L8 OR L9 OR L10)  
L88 269 SEA ABB-ON L11  
E MORPHINE/CT  
L89 19705 SEA ABB-ON MORPHINE/CT  
E FENTANYL/CT  
L90 11240 SEA ABB-ON FENTANYL/CT  
E SUFENTANIL/CT  
L91 2280 SEA ABB-ON SUFENTANIL/CT  
E ALFENTANIL/CT  
L92 2680 SEA ABB-ON ALFENTANIL/CT  
E OXYMORPHONE/CT  
L93 252 SEA ABB-ON OXYMORPHONE/CT  
E HYDROMORPHONE/CT

74

L94 866 SEA ABB-ON HYDROMORPHONE/CT  
E OXYCODONE/CT  
L95 986 SEA ABB-ON OXYCODONE/CT  
E OPIOID AGONIST/CT  
L96 9 SEA ABB-ON (L85 AND L86) OR ((L85 OR L86) AND (L87 OR L89 OR  
L90 OR L91 OR L92 OR L93 OR L94) AND (L88 OR L95))  
L97 125676 SEA ABB-ON COMB./CT  
L98 433001 SEA ABB-ON DRUG INTERACTIONS/CC  
L99 88 SEA ABB-ON ((L97 OR L98) AND (L87 OR L89 OR L90 OR L91 OR L92  
OR L93 OR L94) AND (L88 OR L95))  
L100 31287 SEA ABB-ON ASTHMA OR BRONCHIECTASIS OR BRONCHI7(2A)DILATATION  
OR KARTAGENER OR TUBERCULOSIS  
L101 3808 SEA ABB-ON COPD OR CHRONIC OBSTRUCTIVE(W) (LUNG OR PULMONARY  
OR RESPIRATORY)  
L102 24212 SEA ABB-ON BRONCHITIS OR BRONCHOPNEUMONIA OR PNEUMONIA OR  
LARYNGITIS OR SINUSITIS OR EMPHYSEMA  
L103 1971 SEA ABB-ON FIBROSING ALVEOLITIS OR FIBROSIS(A) (LUNG OR  
PULMONARY OR RESPIRATORY)  
L104 951 SEA ABB-ON SARCOIDOSIS  
L105 17785 SEA ABB-ON (LUNG OR PULMONARY OR RESPIRATORY) (2A) (CANCER# OR  
NEOPLAS7 OR CARCINOMA#)  
L106 433 SEA ABB-ON SLEEP APNEA  
L107 4 SEA ABB-ON ((L97 OR L98) AND (L87 OR L89 OR L90 OR L91 OR L92  
OR L93 OR L94) AND (L88 OR L95)) AND (L100 OR L101 OR L102 OR  
L103 OR L104 OR L105 OR L106)  
D TRIAL 1-4

FILE 'STNGUIDE' ENTERED AT 10:34:45 ON 14 DEC 2006

FILE 'WPIX' ENTERED AT 10:36:41 ON 14 DEC 2006

L108 79 SEA ABB-ON PACE G7/AU  
L109 2413 SEA ABB-ON SMITH M7/AU  
L110 1 SEA ABB-ON L108 AND L109  
D TRIAL

FILE 'STNGUIDE' ENTERED AT 10:37:23 ON 14 DEC 2006

FILE 'WPIX' ENTERED AT 10:38:56 ON 14 DEC 2006

E B04-A04-ALL/MC  
E B07-H-ALL/MC  
E B12-M10A-ALL/MC  
E B12-M10C-ALL/MC  
E B14-C01-ALL/MC  
E B14-H01-ALL/MC  
E B14-H01N-ALL/MC  
E B14-J02-ALL/MC  
E B14-K01-ALL/MC  
E B14-L01-ALL/MC  
E B14-S09-ALL/MC

FILE 'STNGUIDE' ENTERED AT 10:39:14 ON 14 DEC 2006

FILE 'WPIX' ENTERED AT 10:41:48 ON 14 DEC 2006

L111 3147 SEA ABB-ON MORPHINE/B1,ABEX OR FENTANYL/B1,ABEX OR ALFENTANIL/  
B1,ABEX OR SUFENTANIL/B1,ABEX OR OXYMORPHONE/B1,ABEX OR  
MRZ2593/B1,ABEX OR MRZ 2593/B1,ABEX OR HYDROMORPHONE/B1,ABEX  
E OXYCODONE/CN  
L112 4 SEA ABB-ON OXYCODONE7/CN  
L113 431 SEA ABB-ON L112/DCR  
SEL L112 SDRN,SDCH,DCSE

75

L114 4 SEA ABB-ON (RABAGO/SDCN OR RACDH7/SDCN OR RAOPCO/SDCN OR  
R06854/SDCN OR R16301/SDCN OR 103043-1-0-0/DCSE OR 103043-1-1-0  
/DCSE OR 103043-1-2-0/DCSE OR 758270-1-0-0/DCSE)  
L115 435 SEA ABB-ON L114 OR L113  
L116 513 SEA ABB-ON OXYCODONE/B1,ABEX  
L117 198 SEA ABB-ON MU OPIOIDS/B1,ABEX  
L118 186 SEA ABB-ON KAPPA/B1,ABEX(1W) OPIOIDS/B1,ABEX  
L119 12146 SEA ABB-ON B14-L01/MC OR C14-L01/MC  
L120 100 SEA ABB-ON L117(2A)AGONIST#B1,ABEX OR (L117 AND L119)  
L121 102 SEA ABB-ON L118(2A)AGONIST#B1,ABEX OR (L118 AND L119)  
L122 486502 SEA ABB-ON (M782 OR P867)/(M0,M1,M2,M3,M4,M5,M6 OR A61K045/IPC  
OR B12-C09 OR C12-C09 OR B14-S09 OR C14-S09)/MC  
L123 4 SEA ABB-ON (L108 OR L109) AND (L111 OR L120) AND (L115 OR  
L116 OR L121) AND L122  
L124 28604 SEA ABB-ON ASTHMA/B1,ABEX OR BRONCHIECTASIS/B1,ABEX OR  
BRONCHI7/B1,ABEX(2A)DILATATION/B1,ABEX OR KARTAGENER/B1,ABEX  
OR TUBERCULOSIS/B1,ABEX  
L125 5007 SEA ABB-ON COPD/B1,ABEX OR CHRONIC OBSTRUCTIVE/B1,ABEX(W) (LUNG  
/B1,ABEX OR PULMONARY/B1,ABEX OR RESPIRATORY/B1,ABEX)  
L126 11360 SEA ABB-ON BRONCHITIS/B1,ABEX OR BRONCHOPNEUMONIA/B1,ABEX OR  
PNEUMONIA/B1,ABEX OR LARYNGITIS/B1,ABEX OR SINUSITIS/B1,ABEX  
OR EMPHYSEMA/B1,ABEX  
L127 2462 SEA ABB-ON FIBROSING ALVEOLITIS/B1,ABEX OR FIBROSIS/B1,ABEX(A)  
(LUNG/B1,ABEX OR PULMONARY/B1,ABEX OR RESPIRATORY/B1,ABEX)  
L128 3624 SEA ABB-ON SARCOIDOSIS/B1,ABEX OR SLEEP APNEA#B1,ABEX  
L129 8806 SEA ABB-ON (LUNG/B1,ABEX OR PULMONARY/B1,ABEX OR RESPIRATORY/B  
1,ABEX) (2A) (CANCER#B1,ABEX OR NEOPLAS7/B1,ABEX OR CARCINOMA#B  
1,ABEX)  
L130 26 SEA ABB-ON (L111 OR L120) AND (L115 OR L116 OR L121) AND L122  
AND (L124 OR L125 OR L126 OR L127 OR L128 OR L129)  
L131 25 SEA ABB-ON L130 NOT (L110 OR L123)  
D TRIAL 1-8  
L132 20 SEA ABB-ON SUBANALGES7/B1,ABEX OR SUB ANALGES7/B1,ABEX  
L133 1 SEA ABB-ON L132 AND L130  
D TRIAL  
D KWIC L131 6-10  
D KWIC L131 11-13

FILE 'WPIX' ENTERED AT 10:55:27 ON 14 DEC 2006

D KWIC L131 11-13

FILE 'WPIX' ENTERED AT 10:56:51 ON 14 DEC 2006

L134 1 SEA ABB-ON L120 AND L121 AND L122 AND (L124 OR L125 OR L126  
OR L127 OR L128 OR L129)  
L135 20 SEA ABB-ON L115 AND L111 AND L122 AND (L124 OR L125 OR L126  
OR L127 OR L128 OR L129)  
D KWIC L133  
L136 299 SEA ABB-ON ((L111 OR L117)) (5A) ((L116 OR L121)) (5A) (COMB7/B1,AB  
EX OR CODRUG7/B1,ABEX OR COADMIN7/B1,ABEX OR CONCOMITANT7/B1,AB  
EX OR CONCURRENT7/B1,ABEX OR BLEND7/B1,ABEX OR MIX7/B1,ABEX)  
L137 18 SEA ABB-ON L136 AND L122 AND (L124 OR L125 OR L126 OR L127 OR  
L128 OR L129)  
D QUS  
L138 84 SEA ABB-ON L118(2A)AGONIST#B1,ABEX  
L139 61 SEA ABB-ON L117(2A)AGONIST#B1,ABEX  
L140 384 SEA ABB-ON ((L111 OR L139)) (5A) ((L116 OR L138))  
L141 10 SEA ABB-ON L140(5A) (COMB7/B1,ABEX OR CODRUG7/B1,ABEX OR  
COADMIN7/B1,ABEX OR CONCOMITANT7/B1,ABEX OR CONCURRENT7/B1,ABEX  
OR BLEND7/B1,ABEX OR MIX7/B1,ABEX)  
L142 2 SEA ABB-ON L141 AND (L124 OR L125 OR L126 OR L127 OR L128 OR

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10/661458

L143 35 SEA ABB-ON L140 AND L122 AND (L174 OR L125 OR L126 OR L127 OR L128 OR L129)  
FILE 'MEDLINE' ENTERED AT 11:04:27 ON 14 DEC 2006  
D SAVED  
ACT ARN458MEDAU/A  
-----  
L144( 94)SEA FILE-MEDLINE ABB-ON PACE G7/AU  
L145( 10732)SEA FILE-MEDLINE ABB-ON SMITH M7/AU  
L146( 0)SEA FILE-MEDLINE ABB-ON L144 AND L145  
L147( 28104)SEA FILE-MEDLINE ABB-ON MORPHINE/CT  
L148( 10382)SEA FILE-MEDLINE ABB-ON FENTANYL-NT/CT  
L149( 294)SEA FILE-MEDLINE ABB-ON OXYMORPHONE/CT  
L150( 704)SEA FILE-MEDLINE ABB-ON HYDROMORPHONE/CT  
L151( 540)SEA FILE-MEDLINE ABB-ON OXYCODONE/CT  
L152( 124991)SEA FILE-MEDLINE ABB-ON LUNG DISEASES, OBSTRUCTIVE-NT/CT  
L153( 5936)SEA FILE-MEDLINE ABB-ON BRONCHIECTASIS-NT/CT  
L154( 57086)SEA FILE-MEDLINE ABB-ON TUBERCULOSIS, PULMONARY-NT/CT  
L155( 3460)SEA FILE-MEDLINE ABB-ON BRONCHOPNEUMONIA/CT  
L156( 3610)SEA FILE-MEDLINE ABB-ON LARYNGITIS-NT/CT  
L157( 11628)SEA FILE-MEDLINE ABB-ON SINUSITIS-NT/CT  
L158( 13172)SEA FILE-MEDLINE ABB-ON PULMONARY FIBROSIS/CT  
L159( 1561)SEA FILE-MEDLINE ABB-ON SARCOIDOSIS, PULMONARY/CT  
L160( 113814)SEA FILE-MEDLINE ABB-ON LUNG NEOPLASMS-NT/CT  
L161( 12706)SEA FILE-MEDLINE ABB-ON SLEEP APNEA SYNDROMES-NT/CT  
L162( 0)SEA FILE-MEDLINE ABB-ON (L144 OR L145) AND (L147 OR L148 OR L1  
L163 0 SEA ABB-ON L146 OR L162  
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ACT ARN458MED1/A  
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L164( 28104)SEA FILE-MEDLINE ABB-ON MORPHINE/CT  
L165( 10382)SEA FILE-MEDLINE ABB-ON FENTANYL-NT/CT  
L166( 294)SEA FILE-MEDLINE ABB-ON OXYMORPHONE/CT  
L167( 704)SEA FILE-MEDLINE ABB-ON HYDROMORPHONE/CT  
L168( 540)SEA FILE-MEDLINE ABB-ON OXYCODONE/CT  
L169( 124991)SEA FILE-MEDLINE ABB-ON LUNG DISEASES, OBSTRUCTIVE-NT/CT  
L170( 5936)SEA FILE-MEDLINE ABB-ON BRONCHIECTASIS-NT/CT  
L171( 57086)SEA FILE-MEDLINE ABB-ON TUBERCULOSIS, PULMONARY-NT/CT  
L172( 3460)SEA FILE-MEDLINE ABB-ON BRONCHOPNEUMONIA/CT  
L173( 3610)SEA FILE-MEDLINE ABB-ON LARYNGITIS-NT/CT  
L174( 11628)SEA FILE-MEDLINE ABB-ON SINUSITIS-NT/CT  
L175( 13172)SEA FILE-MEDLINE ABB-ON PULMONARY FIBROSIS/CT  
L176( 1561)SEA FILE-MEDLINE ABB-ON SARCOIDOSIS, PULMONARY/CT  
L177( 113814)SEA FILE-MEDLINE ABB-ON LUNG NEOPLASMS-NT/CT  
L178( 12706)SEA FILE-MEDLINE ABB-ON SLEEP APNEA SYNDROMES-NT/CT  
L179 1 SEA ABB-ON (L164 OR L165 OR L166 OR L167) AND L168 AND (L169  
OR L170 OR L171 OR L172 OR L173 OR L174 OR L175 OR L176 OR  
L177 OR L178)  
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ACT ARN458MED2/A  
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L180( 28104)SEA FILE-MEDLINE ABB-ON MORPHINE/CT  
L181( 10382)SEA FILE-MEDLINE ABB-ON FENTANYL-NT/CT  
L182( 294)SEA FILE-MEDLINE ABB-ON OXYMORPHONE/CT  
L183( 704)SEA FILE-MEDLINE ABB-ON HYDROMORPHONE/CT  
L184( 540)SEA FILE-MEDLINE ABB-ON OXYCODONE/CT  
L185( 108974)SEA FILE-MEDLINE ABB-ON DRUG INTERACTIONS-NT/CT  
L186( 42787)SEA FILE-MEDLINE ABB-ON DRUG COMBINATIONS/CT  
L187( 97253)SEA FILE-MEDLINE ABB-ON DRUG THERAPY, COMBINATION/CT

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L188( 15)SEA FILE-MEDLINE ABB-ON (L180 OR L181 OR L182 OR L183) AND L18  
L189 3 SEA ABB-ON L188 AND SYNERG?  
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ACT ARN458MED3/A  
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L190( 108974)SEA FILE-MEDLINE ABB-ON DRUG INTERACTIONS-NT/CT  
L191( 42787)SEA FILE-MEDLINE ABB-ON DRUG COMBINATIONS/CT  
L192( 97253)SEA FILE-MEDLINE ABB-ON DRUG THERAPY, COMBINATION/CT  
L193( 1136)SEA FILE-MEDLINE ABB-ON RECEPTORS, OPIOID, MU/CT(L)AG/CT  
L194( 881)SEA FILE-MEDLINE ABB-ON RECEPTORS, OPIOID, KAPPA/CT(L)AG/CT  
L195( 23)SEA FILE-MEDLINE ABB-ON L193 AND L194 AND (L198 OR L199 OR L19  
L196( 240557)SEA FILE-MEDLINE ABB-ON DOSE-RESPONSE RELATIONSHIP, DRUG/CT  
L197 1 SEA ABB-ON L195 AND L196 AND CONDITIONING, OPERANT/CT  
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ACT ARN458MED4/A  
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L198( 28104)SEA FILE-MEDLINE ABB-ON MORPHINE/CT  
L199( 10382)SEA FILE-MEDLINE ABB-ON FENTANYL-NT/CT  
L200( 294)SEA FILE-MEDLINE ABB-ON OXYMORPHONE/CT  
L201( 704)SEA FILE-MEDLINE ABB-ON HYDROMORPHONE/CT  
L202( 540)SEA FILE-MEDLINE ABB-ON OXYCODONE/CT  
L203( 1136)SEA FILE-MEDLINE ABB-ON RECEPTORS, OPIOID, MU/CT(L)AG/CT  
L204( 881)SEA FILE-MEDLINE ABB-ON RECEPTORS, OPIOID, KAPPA/CT(L)AG/CT  
L205( 488)SEA FILE-MEDLINE ABB-ON (L198 OR L199 OR L200 OR L201 OR L203)  
L206( 8267)SEA FILE-MEDLINE ABB-ON COUGH/CT  
L207 1 SEA ABB-ON L205 AND L206  
-----  
FILE 'STNGUIDE' ENTERED AT 11:05:43 ON 14 DEC 2006  
FILE 'CAPLUS' ENTERED AT 11:06:43 ON 14 DEC 2006  
D QUE L1  
D QUE L45  
L208 5 SEA ABB-ON (L1 OR L45)  
FILE 'EMBASE' ENTERED AT 11:06:46 ON 14 DEC 2006  
D QUE L81  
FILE 'DRUGU' ENTERED AT 11:06:47 ON 14 DEC 2006  
D QUE L96  
FILE 'WPIX' ENTERED AT 11:06:48 ON 14 DEC 2006  
D QUE L110  
D QUE L123  
FILE 'MEDLINE' ENTERED AT 11:06:50 ON 14 DEC 2006  
D QUE L163  
FILE 'DRUGU, CAPLUS, EMBASE' ENTERED AT 11:07:13 ON 14 DEC 2006  
L209 15 DUP REM L96 L208 L81 (4 DUPLICATES REMOVED)  
ANSWERS '1-9' FROM FILE DRUGU  
ANSWERS '10-13' FROM FILE CAPLUS  
ANSWERS '14-15' FROM FILE EMBASE  
D IBIB ED ABS 1-15  
FILE 'STNGUIDE' ENTERED AT 11:07:44 ON 14 DEC 2006  
FILE 'CAPLUS' ENTERED AT 11:10:12 ON 14 DEC 2006  
D QUE L1  
D QUE L45

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L210 5 SEA ABB-ON (L1 OR L45)  
FILE 'EMBASE' ENTERED AT 11:10:14 ON 14 DEC 2006  
D QUE L81  
FILE 'DRUGU' ENTERED AT 11:10:15 ON 14 DEC 2006  
D QUE L96  
FILE 'WPIX' ENTERED AT 11:10:16 ON 14 DEC 2006  
D QUE L110  
D QUE L123  
L211 4 SEA ABB-ON (L110 OR L123)  
FILE 'MEDLINE' ENTERED AT 11:10:19 ON 14 DEC 2006  
D QUE L163  
FILE 'DRUGU, CAPLUS, WPIX, EMBASE' ENTERED AT 11:10:37 ON 14 DEC 2006  
L212 16 DUP REM L96 L210 L211 L81 (7 DUPLICATES REMOVED)  
ANSWERS '1-9' FROM FILE DRUGU  
ANSWERS '10-13' FROM FILE CAPLUS  
ANSWER '14' FROM FILE WPIX  
ANSWERS '15-16' FROM FILE EMBASE  
D IBIB ED ABS 1-16  
FILE 'STNGUIDE' ENTERED AT 11:11:03 ON 14 DEC 2006  
FILE 'CAPLUS' ENTERED AT 11:12:31 ON 14 DEC 2006  
D QUE L41  
D QUE L44  
L213 5 SEA ABB-ON (L41 OR L44) NOT L210  
FILE 'EMBASE' ENTERED AT 11:12:33 ON 14 DEC 2006  
D QUE L82  
D QUE L84  
L214 2 SEA ABB-ON L84 NOT L81  
FILE 'DRUGU' ENTERED AT 11:12:35 ON 14 DEC 2006  
D QUE L107  
L215 4 SEA ABB-ON L107 NOT L96  
FILE 'WPIX' ENTERED AT 11:12:38 ON 14 DEC 2006  
D QUE L134  
D QUE L142  
L216 2 SEA ABB-ON (L134 OR L142) NOT L211  
FILE 'MEDLINE' ENTERED AT 11:12:43 ON 14 DEC 2006  
D QUE L189  
D QUE L197  
D QUE L207  
D QUE L179  
L217 6 SEA ABB-ON (L189 OR L197 OR L207 OR L179)  
FILE 'MEDLINE, DRUGU, CAPLUS, WPIX, EMBASE' ENTERED AT 11:13:15 ON 14 DEC  
2006  
L218 19 DUP REM L217 L215 L213 L216 L314 (0 DUPLICATES REMOVED)  
ANSWERS '1-6' FROM FILE MEDLINE  
ANSWERS '7-10' FROM FILE DRUGU  
ANSWERS '11-15' FROM FILE CAPLUS  
ANSWERS '16-17' FROM FILE WPIX  
ANSWERS '18-19' FROM FILE EMBASE

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D IALL 1-10  
D IBIB ED ABS HIT 11-15  
D IBIB ABOQ TECH HITSTR 16-17  
D IALL 18-19  
FILE 'HOME' ENTERED AT 11:13:55 ON 14 DEC 2006

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